Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russel Examiner #: 62785 Date: 2-24-2005
Art Unit: 1654 Phone Number 571-272-0969 Serial Number: 10/758,717
Mail Box and Bldg/Room Location: REM 3C18 (mailbox), 3D19 (office) Results Format Preferred (circle): PAPER DISK E-MAIL
If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

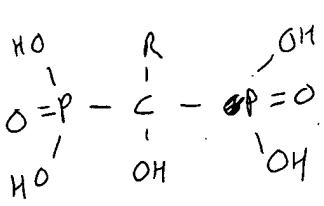
Title of invention: Method of Modifying The Release Profile Of Sustained Release Compositions

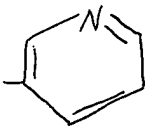
Inventors (please provide full names): J. Dasch, M. Riley

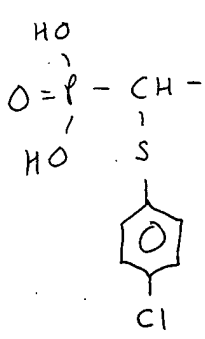
Earliest Priority Filing Date: 1-16-2004

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the following structures



where R is $-CH_2$  , $-CH_2-CH_2-CH_2-NH_2$, $-CH_2-CH_2-NH_2$, or $-CH_3$.



I'm looking for these compounds in pharmaceutical compositions, in particular in combination with biodegradable polymeric carriers, esp. poly(lactide-co-glycolide), in the form of a sustained release/controlled release composition.

Thank you. JER

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed:	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time	Other	Other (specify)

PTO-1590 (8-01)

Russell
10/758717

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=> d l3 que stat;fil medl,biosis,embase,hcapl;s l3
L1              STR
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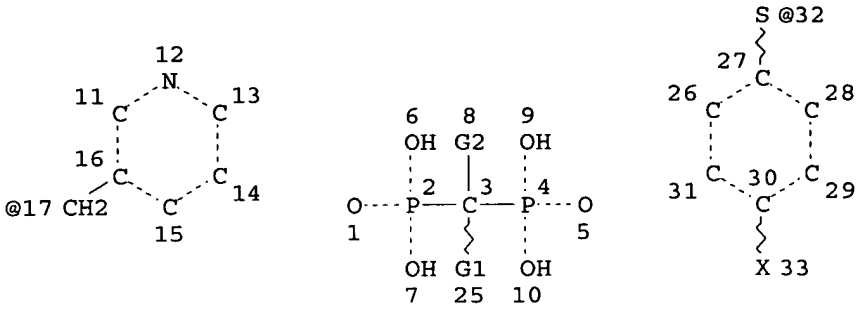

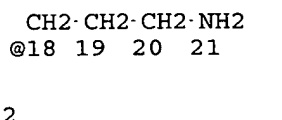


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VAR G1=17/22/18/ME/32
VAR G2=H/OH
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  33

STEREO ATTRIBUTES: NONE
L3           595 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED   5922 ITERATIONS                      595 ANSWERS
SEARCH TIME: 00.00.01


COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY     SESSION
FULL ESTIMATED COST                           164.34     164.55

FILE 'MEDLINE' ENTERED AT 14:18:26 ON 25 MAR 2005

FILE 'BIOSIS' ENTERED AT 14:18:26 ON 25 MAR 2005
Copyright (c) 2005 The Thomson Corporation

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FILE 'HCAPLUS' ENTERED AT 14:18:26 ON 25 MAR 2005
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L4          3749 FILE MEDLINE
L5          1875 FILE BIOSIS


Searched by: Mary Hale 571-272-2507 REM 1D86
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L6          9510 FILE EMBASE
L7          6759 FILE HCAPLUS

TOTAL FOR ALL FILES
L8         21893 L3

=> s (sustain? or timed or control?)(4a)releas? or polymer? carrier? or poly
lactide co glycolide or polygalactin 910 or glycolic lactic acid polyester)
UNMATCHED RIGHT PARENTHESIS 'POLYESTER)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (sustain? or timed or control?)(4a)releas? or polymer? carrier? or poly
lactide co glycolide or polygalactin 910 or glycolic lactic acid polyester
L9         17682 FILE MEDLINE
L10        23509 FILE BIOSIS
L11        29691 FILE EMBASE
L12        46623 FILE HCAPLUS

TOTAL FOR ALL FILES
L13       117505 (SUSTAIN? OR TIMED OR CONTROL?)(4A) RELEAS? OR POLYMER? CARRIER?
                  OR POLY LACTIDE CO GLYCOLIDE OR POLYGALACTIN 910 OR GLYCOLIC
                 LACTIC ACID POLYESTER

=> s l8 and l13
L14            8 FILE MEDLINE
L15            1 FILE BIOSIS
L16           40 FILE EMBASE
L17           72 FILE HCAPLUS

TOTAL FOR ALL FILES
L18          121 L8 AND L13

=> s l18 and (pharm? or compos?)
L19            2 FILE MEDLINE
L20            1 FILE BIOSIS
L21           30 FILE EMBASE
L22           51 FILE HCAPLUS

TOTAL FOR ALL FILES
L23           84 L18 AND (PHARM? OR COMPOS?)

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24            79 DUP REM L23 (5 DUPLICATES REMOVED)

=> d 1-79 ibib abs hitstr;s l8 and (dasch j?/au or riley m?/au)
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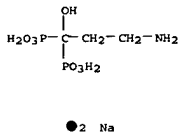
Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 1 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:216714 HCAPLUS
TITLE: **Compositions** and methods for delivery of biologically active agents
INVENTOR(S): Khoo, Shui-mei; Boyd, Benjamin James; Whittaker, Darryl Vanstone; Davey, Gregory Andrew
PATENT ASSIGNEE(S): DBL Australia Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021046	A1	20050310	WO 2004-AU1181	20040901
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
AU 2003-904717 A 20030901
AU 2003-904719 A 20030901

AB The present invention provides methods and **compns.** for the delivery of a biol. active agent to a biol. system. The **compns.** include the active agent and a lyotropic phase and release of the active agent to the biol. system is modified by the lyotropic phase. Thus, a formulation contained irinotecan and 2,3-dihydroxypropionic acid 3,7,11,15-tetramethyl hexadecyl ester and water. A **sustained release** of the drug from the formulation was achieved.
IT INDEXING IN PROGRESS
IT **57248-88-1**, Disodium pamidronate
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns.** for delivery of biol. active agents)
RN 57248-88-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L24 ANSWER 1 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L24 ANSWER 2 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:119884 HCAPLUS
DOCUMENT NUMBER: 142:204864
TITLE: Medical implants coated with porous carbon surfaces carrying drugs
INVENTOR(S): Rathenow, Joerg; Asgari, Soheil; Ban, Andreas
PATENT ASSIGNEE(S): Blue Membranes GmbH, Germany
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10333099	A1	20050210	DE 2003-10333099	20030721
DE 202004009061	U1	20040916	DE 2004-202004009061	20040528
WO 2004105826	A2	20041209	WO 2004-EP5785	20040528
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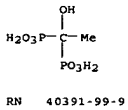
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

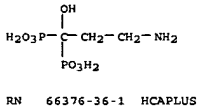
PRIORITY APPLN. INFO.:
DE 2003-10324415 A1 20030528
DE 2003-10333098 A1 20030721
DE 2003-10333099 A1 20030721

AB The invention concerns a method for the preparation of medical implants with functionalized surfaces involving the steps: (a)preparation of medical implant that is at least partially coated with a carbon-containing layer; (b) activation of the carbon-containing layer by forming a pores on the surface; (c) functionalization of the activated, carbon-containing surface. The carbon-containing layer is **composed** of pyrolytically prepared carbon, carbon deposited by CVD or PVD process, sputtered carbon, metal carbides, metal carbonitrides, metal oxynitrides, metal oxycarbides or their combinations. The carbon-containing layers are activated by oxidation with air, oxygen, dinitrogen oxide, and oxidizing acids, also at elevated temperature A reduction process can also be used for activation. Activated surfaces are functionalized by loading one or more drugs, microorganisms or cells onto the surface. Activated surfaces can be sealed in a CVD or CVI (chemical vapor infiltration) process. The implants are prepared from carbon, carbon fibers, ceramics, glass, metals, alloys, artificial bone, stone, minerals. Artificial blood vessels, stents, coronary stents, peripheral stents,

L24 ANSWER 2 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
orthopedic implants, bone and joint prosthesis, artificial heart, heart valves, s.c., and i.m. implants can be activated and functionalized.
IT **2809-21-4**, Etidronic acid **40391-99-9 66376-36-1**
, Alendronic acid **89987-06-4**, Tiludronic acid
105462-24-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical implants coated with porous carbon surfaces carrying drugs)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
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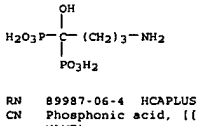
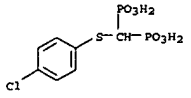
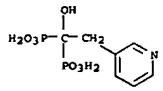


RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

L24 ANSWER 2 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:119883 HCAPLUS
DOCUMENT NUMBER: 142:204863
TITLE: Biocompatible coated medical implants with a carbon layer and method for preparation
INVENTOR(S): Rathenow, Joerg; Asgari, Soheil; Ban, Andreas
PATENT ASSIGNEE(S): Blue Membranes GmbH, Germany
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10333098	A1	20050210	DE 2003-10333098	20030721
DE 202004009060	U1	20040916	DE 2004-202004009060	20040510
WO 2004101017	A2	20041125	WO 2004-EP4985	20040510
WO 2004101017	A3	20050303		

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DE 202004009061	U1	20040916	DE 2004-202004009061	20040528
WO 2004105826	A2	20041209	WO 2004-EP5785	20040528

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PRIORITY APPLN. INFO.:	DE 2003-10322182	A1 20030516
	DE 2003-10324415	A1 20030528
	DE 2003-10333098	A1 20030721
	DE 2003-10333099	A1 20030721

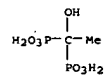
AB The invention concerns a method for the preparation of biocompatible coatings for implants, and medical goods composing the steps (a) coating the medical good at least partially with a polymer film using a coating process; (b) heating the polymer film in an oxygen-free atmospheric at 200-2500 °C to obtain a carbon layer on the medical good. The medical goods are heat resistant; they are prepared from carbon, carbon fibers, ceramics,

L24 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

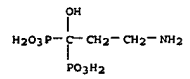
glass, metals, alloys, artificial bone, stone, minerals; during heating they are transferred to their thermostable state. Artificial blood vessels, stents, coronary stents, peripheral stents, orthopedic implants, bone and joint prosthesis, artificial heart, heart valves, s.c., and i.m. implants can be coated. Other coating methods, e.g. dipping, spraying, printing can be applied. Several carbon layers with various porosity can be formed; biocompatible, biodegradable, non-biodegradable polymer layers can be placed on top of the carbon layers; drugs can be adsorbed onto the layers.

IT **2809-21-4**, Etidronic acid **40391-99-9** **66376-36-1**, Alendronic acid **89987-06-4**, Tiludronic acid **105462-24-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biocompatible coated medical implants with a carbon layer and method for preparation)

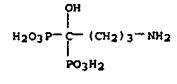
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

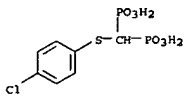


RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

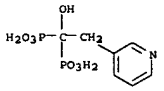


RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)

L24 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 4 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005011145 EMBASE
TITLE: Electrolytic deposition of calcium etidronate drug coating on titanium substrate.
AUTHOR: Duan K.; Fan Y.; Wang R.
CORPORATE SOURCE: R. Wang, Department of Materials Engineering, University of British Columbia, 309-6350 Stores Road, Vancouver, BC V6T 1Z4, Canada. rzwang@interchange.ubc.ca
SOURCE: Journal of Biomedical Materials Research - Part B Applied Biomaterials, (15 Jan 2005) 72/1 (43-51). Refs: 31 ISSN: 0021-9304 CODEN: JBMRGL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Wear debris-induced osteolysis is the major cause of aseptic loosening and failure of hip implants. One of the promising therapeutic interventions to improve the longevity of hip implants is to administrate bisphosphonate drug to inhibit osteoclastic bone resorption. This study aimed at developing new techniques of directly combining bisphosphonate with implants to achieve local delivery and **controlled release** of the drug. Instead of using soluble sodium salt, we proposed to apply sparingly soluble calcium salt of bisphosphonate as a potential long-term antiosteolysis coating on hip implants. Calcium salt of etidronate, a member of the bisphosphonate family of potent osteoclast inhibitors, was used in this pilot study. By adopting the electrolytic deposition (ELD) technique, which was developed for ceramic coatings including calcium phosphates, we demonstrated that a thin layer of calcium bisphosphonate could be deposited onto titanium surface. The drug coating is amorphous as characterized with X-ray diffraction, and has globular morphology under the scanning electron microscope. Electrospray-ionization mass-spectrometry (ESI-MS) and Fourier-transformed infrared spectroscopy confirmed that the molecular structure of the etidronate (m/z 205, H(3)L(-), the single dissociated form of parent etidronic acid, denoted as H(4)L) was preserved after the ELD process. In vitro release into a " physiological" buffer solution confirmed that the etidronate concentration was limited by its low solubility. The etidronate concentration was 8 x 10(-5) M at day 1 and kept relatively stable at .apprx.6 x 10 (-5) M from day 2 to day 8. The deposition mechanisms of the drug coating and its potential efficacy as an antiosteolytic release source were discussed. .COPYRGT. 2004 Wiley Periodicals, Inc.

L24 ANSWER 5 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

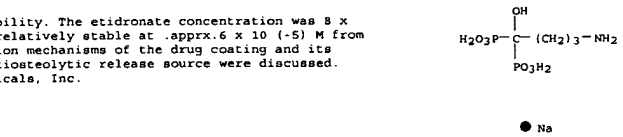
ACCESSION NUMBER: 2004:902159 HCAPLUS
DOCUMENT NUMBER: 141:370572
TITLE: Orally disintegrating tablets containing silicified cellulose
INVENTOR(S): Platteeuw, Johannes Jan; Van den Heuvel, Dennie Johan Marijn
PATENT ASSIGNEE(S): Synthon B.V., Neth.
SOURCE: PCT Int. Appl., 39 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091585	A1	20041028	WO 2004-EP4119	20040416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004265375	A1	20041230	US 2004-824619	20040415
PRIORITY APPLN. INFO.:			US 2003-463027P	P 20030416

AB Silicified microcryst. cellulose is used to provide a tablet with oral disintegration. The tablet contains at least 30% of the silicified microcryst. cellulose and an effective amount of a **pharmaceutically** active agent. For example, orally disintegrating tablets were prepared containing leflunomide 20.00%, silicified microcryst. cellulose (Prosolv) 74.50%, low-substituted hydroxypropyl cellulose 5.0%, and Mg stearate 0.5%.

IT 129318-43-0, Alendronate sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orally disintegrating tablets containing silicified microcryst. cellulose)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L24 ANSWER 5 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

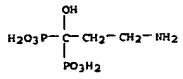
L24 ANSWER 6 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:433684 HCAPLUS
DOCUMENT NUMBER: 140:429037
TITLE: High viscosity liquid controlled drug delivery system and medical or surgical device
INVENTOR(S): Gibson, John W.; Miller, Stacey S.; Middleton, John C.; Tipton, Arthur J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 699,002. CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

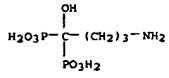
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004101557	A1	20040527	US 2002-316441	20021210
US 5747058	A	19980505	US 1995-474337	19950607
US 6413536	B1	20020702	US 1999-385107	19990827
WO 2004052336	A2	20040624	WO 2003-US39311	20031210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1995-474337	A2 19950607
			US 1995-478450	B2 19950607
			US 1997-944022	A2 19970915
			US 1999-385107	A3 19990827
			US 2000-699002	A2 20001026
			US 2002-316441	A 20021210

AB The present invention relates to novel nonpolymeric compds. and compns. that form liquid, high viscosity materials suitable for the delivery of biol. active substances in a controlled fashion, and for use as medical or surgical devices. The materials can optionally be diluted with a solvent to form a material of lower viscosity, rendering the material easy to administer. This solvent may be water insol. or water soluble, where the water soluble solvent rapidly diffuses or migrates away from the material in vivo, leaving a higher viscosity liquid material. 1,6-Hexanediol lactate ε-hydroxycaproic acid produced in was dissolved in N-methylpyrrolidone at a weight ratio of 70:30. Bupivacaine base (10%) was then added to this mixture. Drops weighing approx. 100 mg were precipitated into 40 mL buffer. At 4 h, around 4.1 weight% of the bupivacaine contained in the precipitated drop had been released. At 24 h, around 8.6 weight%

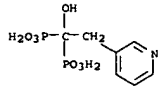
L24 ANSWER 6 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
of the bupivacaine had been released.
IT **40391-99-9 66376-36-1**, Alendronate **105462-24-6**
, Risedronic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high viscosity liquid controlled drug delivery system and medical or surgical device)
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

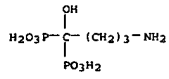


L24 ANSWER 7 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:219836 HCAPLUS
DOCUMENT NUMBER: 140:259061
TITLE: **Controlled release** dosage forms with core tablet sheathed in an annular body of compressed powder or granular material
INVENTOR(S): Lerner, E. Itzhak; Rosenberger, Vered; Aqua, Ofer; Flashner-Barak, Moshe
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 291,619, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004052843	A1	20040318	US 2003-379338		20030303
BR 2002015413	A	20041214	BR 2002-15413		20021112
US 2003206954	A1	20031106	US 2003-419536		20030421
PRIORITY APPLN. INFO.:			US 2001-342442P	P	20011224
			US 2002-361821P	P	20020304
			US 2002-291619	B2	20021112
			WO 2002-US63081	W	20021112

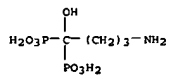
AB The present invention provides **controlled release pharmaceutical** dosage forms for oral administration in which a core tablet is sheathed in an annular body of compressed powder or granular material. A preferred embodiment of the zero-order release **pharmaceutical** dosage form is a solid **pharmaceutical** dosage form which reduces contact of the active ingredient in solid form with the mucosa lining the gastrointestinal tract, which is particularly advantageous for delivering an ulcerative drug. The drug layer may be recessed from the opening of the annular body on one or both sides, and the drug layer is recessed from the surface so that any contact, whether with hands or with the mucosa, is with the walls of the annular body. The annular body is preferably made of non ulcerative and non sensitive **pharmaceutical** ingredients such as hydroxypropyl cellulose, hydroxypropyl methylcellulose, microcryst. cellulose, starch, lactose, sugars, polyvinyl pyrrolidone, calcium phosphate and any other regular tablet excipients. A process for making the zero-order release **pharmaceutical** dosage form are also provided.
IT **129318-43-0**, Monosodium alendronate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled release** dosage forms with core tablet sheathed in annular body of compressed powder or granular material)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 7 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

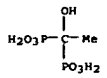
IT **66376-36-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled release** dosage forms with core tablet sheathed in annular body of compressed powder or granular material)
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



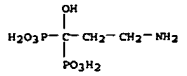
L24 ANSWER 8 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:756044 HCAPLUS
DOCUMENT NUMBER: 141:266048
TITLE: Medical implants with carbon-containing surfaces that are functionalized
PATENT ASSIGNEE(S): Blue Membranes GmbH, Germany
SOURCE: Ger. Gebrauchsmusterschrift, 18 pp.
CODEN: GGXXFR
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
DE 202004009061	U1	20040916	DE 2004-202004009061		20040528
DE 10324415	A1	20041216	DE 2003-10324415		20030528
DE 10333098	A1	20050210	DE 2003-10333098		20030721
DE 10333099	A1	20050210	DE 2003-10333099		20030721
PRIORITY APPLN. INFO.:			DE 2003-10324415	A1	20030528
			DE 2003-10333098	A1	20030721
			DE 2003-10333099	A1	20030721

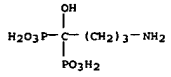
AB The invention concerns medical implants with carbon-containing surfaces that are functionalized; the surfaces are prepared by (a) preparing a medical implant with a carbon-containing surface; (b) activation of the carbon layer by creating porosity; (c) functionalization of the activated, carbon-containing layer. The carbon layer can be prepared by pyrolysis, CVD, PVD, sputtering, ion implantation. The medical devices are prepared from carbon, carbon-**composite** material, glass, ceramics, glass fibers, carbon fibers, metals, stainless steel, titanium, tantalum, platinum, nitinol, alloys, artificial bone, minerals, and their combinations. Artificial blood vessels, stents, coronary stents, peripheral stents, orthopedic implants, artificial hearts and heart valves, artificial bones and joints are prepared The carbon layer is activated with oxidation or reducing agents in the presence of air, oxygen, nitrogen monoxide, oxidative acids; heat and/or ultrasound can be applied. The activated implant surfaces are functionalized with drugs, microorganisms, plant, animal or human cells. The invention also concerns **controlled-release** implanted drug delivery systems.
IT **2809-21-4**, Etidronic acid **40391-99-9 66376-36-1**
, Alendronic acid **89987-06-4**, Tiludronic acid
105462-24-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical implants with carbon-containing surfaces that are functionalized)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



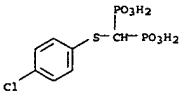
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



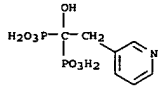
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 9 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004335684 EMBASE
TITLE: **Pharmacological** management of metastatic boney pain.
AUTHOR: Viney R.P.C.; Hayne D.; Ayra M.; Patel H.R.H.
CORPORATE SOURCE: Dr. H.R.H. Patel, Department of Urology, Guys Hospital, St Thomas Street, London SE1 9R, United Kingdom. hrhpatel@doctors.org.uk
SOURCE: Expert Opinion on Pharmacotherapy, (2004) 5/7 (1555-1563). Refs: 39
ISSN: 1465-6566 CODEN: EOPHF7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
033 Orthopedic Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Many malignancies metastasise to the skeleton. This often results in a relatively unique pain process, which dramatically affects a patient's quality of life. With one in three members of the population likely to develop cancer at some stage in their lives, the prevalence of bone metastases is high. Despite the large financial investment on therapies for these patients, treatment is still suboptimal [1]. In this article, the various treatments available are reviewed. Opiates and bisphosphonates, the mainstays in current practise, are covered in detail, and evolving therapies that may shape future management are also discussed. 2004 .COPYRGT. Ashley Publication Ltd.

L24 ANSWER 10 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004393283 EMBASE
TITLE: [Supportive therapy of multiple myeloma]. SUPPORTIVE THERAPIE DES MULTIPLEN MYELOMS.
AUTHOR: Zojer N.; Strasser-Weippl K.; Ludwig H.
CORPORATE SOURCE: Dr. H. Ludwig, Medizinische Abteilung mit Onkologie, Wilhelminenspital, Montleartstrasse 37, 1160 Wien, Austria. Heinz.ludwig@wienkav.at
SOURCE: Onkologe, (2004) 10/8 (843-851). Refs: 28
ISSN: 0947-8965 CODEN: ONKOF4
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB During the last decade, the life expectancy of patients with multiple myeloma has improved significantly, mainly due to more efficient anti-myeloma therapy. In order to preserve a high quality of life throughout the course of the disease, comprehensive supportive therapy is necessary. The most common complications occurring in patients with myeloma are osteolytic bone lesions leading to pain and fractures, hypercalcemia, anemia with fatigue, and infections. For prevention and/or therapy of these complications a variety of measures may be required/including the administration of bisphosphonates, radiation and timely operative stabilization of osteolytic lesions to prevent pathologic fractures, adequate therapy of anemia, tailored pain therapy, rapid treatment, and prophylaxis against possible infections. Treatment success increases the patients' well-being, which is mirrored in improved quality of life.

L24 ANSWER 11 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004487237 EMBASE
TITLE: Symptom management in the older adult.
AUTHOR: Brown J.A.; Von Roenn J.H.
CORPORATE SOURCE: . j-vonroenn@northwestern.edu
SOURCE: Clinics in Geriatric Medicine, (2004) 20/4 (621-640).
Refs: 98
ISSN: 0749-0690 CODEN: CGMEE6
PUBLISHER IDENT.: S 0749-0690(04)00063-1
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 020 Gerontology and Geriatrics
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Palliative care begins at the time of diagnosis of a life-threatening illness and continues beyond the time of death. Defined in the broadest sense, the goal of palliative care is to provide aggressive symptom management and address the psychological and spiritual needs of the patient and the family. This article reviews the management of some symptoms commonly observed in older patients, highlighting treatment considerations specific to the older population. Ultimately the approach to symptoms must be individualized, and treatment decisions must reflect the patient's goals of care. Although symptom management in older patients may be challenging, it is possible to provide care that significantly enhances quality of life throughout the course of illness.

L24 ANSWER 12 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004450001 EMBASE
TITLE: Preparation and evaluation of floating risedronate sodium Gelucire® 39/01 matrices.
AUTHOR: Chauhan B.; Shimpi S.; Mahadik K.R.; Paradkar A.
CORPORATE SOURCE: A. Paradkar, Department of Pharmaceutics, Bharati Vidyapeeth Deemed University, Poona College of Pharmacy, Erandwane, Pune-411038, Maharashtra, India. anant_paradkar@yahoo.com
SOURCE: Acta Pharmaceutica, (2004) 54/3 (205-214).
Refs: 24
ISSN: 1330-0075 CODEN: ACPHEE
COUNTRY: Croatia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 023 Nuclear Medicine
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English; Serbian
AB Incorporation of bisphosphonates in the lipid reduces gastric irritation. Only gastric retention with **sustained release** allows the drug to reach the duodenum and jejunum and improves the availability of bisphosphonates. Risedronate sodium and Gelucire® 39/01 floating matrices were prepared using melt solidification. The **sustained release** floating matrices were evaluated for in vitro and in vivo floating ability and in vitro drug release. Ageing of the matrices was studied by differential scanning calorimetry, hot stage polarizing microscopy, scanning electron microscopy and in vitro drug release. Ageing causes changes in the crystal structure of Gelucire®, which is responsible for an increase in drug release.

L24 ANSWER 13 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004229328 EMBASE
TITLE: **Pharmacokinetic** and **pharmacodynamic** aspects of gastroretentive dosage forms.
AUTHOR: Hoffman A.; Stepensky D.; Lavy E.; Eyal S.; Klausner E.; Friedman M.
CORPORATE SOURCE: A. Hoffman, Department of Pharmaceutics, School of Pharmacy, Hebrew University of Jerusalem, P.O. Box 12065, Jerusalem 91120, Israel. ahoffman@cc.huji.ac.il
SOURCE: International Journal of Pharmaceutics, (11 Jun 2004) 277/1-2 (141-153).
Refs: 28
ISSN: 0378-5173 CODEN: IJPHDE
PUBLISHER IDENT.: S 0378-5173(04)00122-X
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Controlled release** gastroretentive dosage forms (CR-GRDF) enable prolonged and continuous input of the drug to the upper parts of the gastrointestinal (GI) tract and improve the bioavailability of medications that are characterized by a narrow absorption window. CR-GRDF provide a means to utilize all the **pharmacokinetic** (PK) and **pharmacodynamic** (PD) advantages of **controlled release** dosage forms for such drugs. Thus, CR-GRDF may improve therapy with clinically used medications, as well as enable oral administration of drugs, or drug candidates, that hitherto had to be infused parenterally. This manuscript discusses the complexity of the PK and PD factors that influence the treatment benefits of CR-GRDF and summarizes the results of our recent in vivo investigations in animal models (rats and dogs) and in human subjects. We found that a CR-GRDF formulation was superior to the other modes of administration for levodopa and riboflavin, but not for metformin. The PK and PD rationales of GRDFs for the studied drugs are presented and discussed. We conclude that due to the complexity of the PK and PD factors for a certain drug, the rationale for continuous administration obtained by CR-GRDF should be **assessed** and established in vivo. .COPYRGT. 2004 Elsevier B.V. All rights reserved.

L24 ANSWER 14 OF 79 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004297256 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15198426
TITLE: Microencapsulation of hydrophilic drug substances using biodegradable polyesters. Part II: Implants allowing **controlled** drug **release**--a feasibility study using bisphosphonates.
AUTHOR: Weidenauer U; Bodmer D; Kissel T
CORPORATE SOURCE: Department of Pharmaceutics and Biopharmacy, Philipps-University, D-35032 Marburg, Germany.
SOURCE: Journal of microencapsulation, (2004 Mar) 21 (2) 137-49.
Journal code: 8500513. ISSN: 0265-2048.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040617
Last Updated on STN: 20040915
Entered Medline: 20040914
AB The prolonged delivery of hydrophilic drug salts from hydrophobic **polymer carriers** at high drug loading is an ambitious goal. Pamidronate disodium salt (APD) containing implants prepared from spray-dried microparticles were investigated using a laboratory ram extruder. An APD-containing polymer matrix consisting of an APD-chitosan implant embedded in the biodegradable polymer D,L-**poly(lactide-co-glycolide** acid-glucose) (PLG-GLU) was compared with a matrix system with the micronized drug distributed in the PLG-GLU. The APD-chitosan matrix system showed a triphasic release behaviour at loading levels of 6.86 and 15.54% (w/w) over 36 days under in-vitro conditions. At higher loading (31.92%), a drug burst was observed within 6 days due to the formation of pores and channels in the polymeric matrix. In contrast, implants containing the micronized drug showed a more continuous release profile over 48 days up to a loading of 31.78% (w/w). At a drug loading of 46.17% (w/w), a drug burst was observed. Using micronized drug salts and reducing the surface area available for diffusion, parenteral delivery systems for highly water-soluble drug candidates were shown to be technically feasible at high drug loadings.

Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 15 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2005027526 EMBASE
TITLE: [News from drug research and development].
NEUES AUS ARZNEIMITTEL-FORSCHUNG UND -ENTWICKLUNG.
SOURCE: Deutsche Apotheker Zeitung, (23 Dec 2004) 144/52 (21-33).
ISSN: 0011-9857 CODEN: DAZEA2
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: German

L24 ANSWER 16 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004161336 EMBASE
TITLE: Chitosan microspheres as a potential carrier for drugs.
AUTHOR: Sinha V.R.; Singla A.K.; Wadhawan S.; Kaushik R.; Kumria R.; Bansal K.; Dhawan S.
CORPORATE SOURCE: V.R. Sinha, Univ. Inst. of Pharmaceutical Sci., Panjab University, Chandigarh 160014, India. vr_sinha@yahoo.com
SOURCE: International Journal of Pharmaceutics, (15 Apr 2004) 274/1-2 (1-33).
Refs: 205
ISSN: 0378-5173 CODEN: IJPHDE
PUBLISHER IDENT.: S 0378-5173(04)00022-5
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Chitosan is a biodegradable natural polymer with great potential for **pharmaceutical** applications due to its biocompatibility, high charge density, non-toxicity and mucoadhesion. It has been shown that it not only improves the dissolution of poorly soluble drugs but also exerts a significant effect on fat metabolism in the body. Gel formation can be obtained by interactions of chitosans with low molecular counterions such as polyphosphates, sulphates and crosslinking with glutaraldehyde. This gelling property of chitosan allows a wide range of applications such as coating of **pharmaceuticals** and food products, gel entrapment of biochemicals, plant embryo, whole cells, microorganism and algae. This review is an insight into the exploitation of the various properties of chitosan to microencapsulate drugs. Various techniques used for preparing chitosan microspheres and evaluation of these microspheres have also been reviewed. This review also includes the factors that affect the entrapment
efficiency and release kinetics of drugs from chitosan microspheres.
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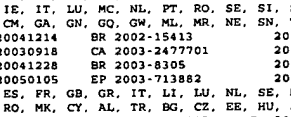
L24 ANSWER 17 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:737555 HCAPLUS
DOCUMENT NUMBER: 139:250322
TITLE: **Controlled release** dosage forms
INVENTOR(S): Lerner, E. Itzhak; Rosenberger, Vered; Aqua, Ofer; Flashner-Barak, Moshe
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa,inc
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075893	A1	20030918	WO 2003-US6591	20030303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
BR 2002015413	A	20041214	BR 2002-15413	20021112
CA 2477701	AA	20030918	CA 2003-2477701	20030303
BR 2003008305	A	20041228	BR 2003-8305	20030303
EP 1492508	A1	20050105	EP 2003-713882	20030303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

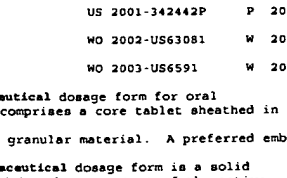
PRIORITY APPLN. INFO.:		
US 2002-361821P	P	20020304
US 2002-291619	A	20021112
US 2001-342442P	P	20011224
WO 2002-US63081	W	20021112
WO 2003-US6591	W	20030303

AB A zero-order release **pharmaceutical** dosage form for oral administration to a patient comprises a core tablet sheathed in an annular
body of compressed powder or granular material. A preferred embodiment of
the zero-order release **pharmaceutical** dosage form is a solid **pharmaceutical** dosage form which reduces contact of the active ingredient in solid form with the mucosa lining the gastrointestinal tract, which is particularly advantageous for delivering an ulcerative drug. A process for making the zero-order release **pharmaceutical** dosage form are also provided. Oxybutynin (50 g), was mixed with anhydrous
lactose (50 g) in a one pot granulator. The granulation solution, 5% KlucelTM LF (21 mL), was added with stirring until thorough mixing was achieved. The granulate was dried in the one pot granulator at 45-50° with for 20 min. The granulate was milled in a Quadro

L24 ANSWER 17 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
ComilTM milling machine using a screen size of 1143 μm. The oxybutynin granulate (27.6 g) was mixed with MethocelTM K15M (19 g), and compressible
sucrose (Nu-TabTM, 52.4 g). Magnesium stearate (1 g) was added with mixing. The blend was compressed into tablets on a single punch tablet machine using 6 mm flat beveled punches to produce tablets weighing about 110 mg and having a hardness of 4 Kp. PEG-4000 was milled and passed through a 500-μm screen. The milled PEG-4000 (24 g), was mixed with Povidone K-30 (5 g), and Ethocel (71 g), for 3 min. Magnesium stearate (1
g), was added and the blend mixed for another 0.5 min. The inner cores, produced above, were pressed within the outer mantle by using this blend and a 9-mm outer cylinder spring loaded core rod tooling. The final product, an annular ring coated tablet with recessed exposed axial faces, had an outer diam. of 9 mm, a total wt. of 350 mg and contained 15 mg oxybutynin.
IT **66376-36-1**, Alendronate **129318-43-0**, Monosodium Alendronate **600116-20-9**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled release** dosage forms)
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

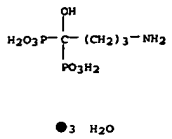


RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)



RN 600116-20-9 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, trihydrate (9CI) (CA INDEX NAME)

L24 ANSWER 17 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●3 H_2O

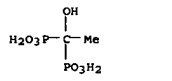
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

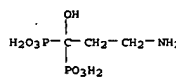
L24 ANSWER 18 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
copolymer and the use thereof. Thus a copolymer was prepd. using the monomers: Me acrylate 40; Et acrylate 30; methacrylic acid 30. An emulsion polymerizate contg. 30% of the copolymer was mixed with 0.85% sodium lauryl sulfate (in relation to the copolymer); the fluid was dried to a film; the film was sol. in an artificial intestinal juice at pH 6.8.

IT **2809-21-4** **40391-99-9** **66376-36-1**, Alendronate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** dosage forms coated with and acrylic copolymers)

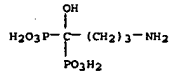
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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L24 ANSWER 18 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:696722 HCAPLUS
DOCUMENT NUMBER: 139:219350
TITLE: **Pharmaceutical** dosage forms coated with and acrylic copolymers
INVENTOR(S): Petereit, Hans-Ulrich; Suefke, Thomas; Meier, Christian; Schnabel, Michael; Blessing, Ingrid; Grimm, Stefan
PATENT ASSIGNEE(S): Roehm G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072087	A1	20030904	WO 2003-EP934	20030130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10208335	A1	20030904	DE 2002-10208335	20020227
CA 2476972	AA	20030904	CA 2003-2476972	20030130
EP 1478352	A1	20041124	EP 2003-711870	20030130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008006	A	20050104	BR 2003-8006	20030130

PRIORITY APPLN. INFO.:		
DE 2002-10208335	A	20020227
WO 2003-EP934	W	20030130

AB The invention relates to a method for producing a **pharmaceutical** dosage form as tablets, pellets and/or in the form of an active ingredient-containing matrix, whereby the tablets, pellets and/or active ingredient-containing matrix contain a **pharmaceutical** active ingredient and a copolymer serving as a coating agent and/or binding agent, and optionally contain a core and **pharmaceutically** common additives. According to the invention, the copolymer, the **pharmaceutical** active ingredient, the optionally present core and/or the **pharmaceutically** common additives are processed using known techniques by melting, injection molding, extrusion, wet granulation, casting, dipping, spreading out, spraying on, or pressing to form tablets, pellets and/or an active ingredient-containing matrix. The inventive method is characterized in that a copolymer is used that consists of 20 to 34 weight % methacrylic acid, 20 to 69 weight % methylacrylate and 0 to 40 weight % ethylacrylate and, optionally, of 0 to 10 weight % of addnl. vinylically copolymerizable monomers with the provision that the glass transition temperature of the copolymer is no higher than 60° according to ISO 11357-2, Item 3.3.3. The invention also relates to the **pharmaceutical** dosage form produced according to this method, said

L24 ANSWER 19 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:511118 HCAPLUS
DOCUMENT NUMBER: 139:90451
TITLE: Zero-order **sustained-release** dosage forms
INVENTOR(S): Heimlich, John M.; Noack, Robert M.; Cox, Steve R.; Ganorkar, Loksidh D.; Verhage, Ronald R.; John, Lee E.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053402	A1	20030703	WO 2002-US41104	20021219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003133982	A1	20030717	US 2002-324719	20021219
EP 1455751	A1	20040915	EP 2002-792508	20021219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002015262	A	20041228	BR 2002-15262	20021219

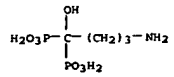
PRIORITY APPLN. INFO.:		
US 2001-342642P	P	20011220
US 2001-342819P	P	20011220
WO 2002-US41104	W	20021219

AB The present invention relates to zero-order **sustained-release** solid dosage forms suitable for administration of a wide range of drugs, especially those that are water-soluble The solid dosage form comprises (a) a matrix core comprising Et cellulose and the active agent and (b) a hydrophobic polymer coating encasing the entire matrix core. Thus, tablets contained clindamycin-HCl 76.44, Et cellulose 18.08, and Mg stearate 0.25%. Extra-granular formulations comprised Ethocel 4.99, and Mg stearate 0.25%. The coating **composition** comprised HPMC 10.8, and Surelease 43.2%.

IT **66376-36-1**, Alendronate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order **sustained-release** dosage forms)

RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 19 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:491052 HCAPLUS
DOCUMENT NUMBER: 139:57948
TITLE: Liquid bisphosphonate formulations for bone disorders
INVENTOR(S): Daifotis, Anastasia G.; Leung, Albert T.; Bergquist, Paul A.; Denker, Andrew
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051373	A1	20030626	WO 2002-US38200	20021126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003139378	A1	20030724	US 2002-305868	20021126
EP 1458400	A1	20040922	EP 2002-784653	20021126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

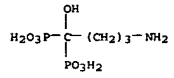
PRIORITY APPLN. INFO.: US 2001-340965P P 20011213
WO 2002-US38200 W 20021126

AB The present invention relates to high dose oral liquid formulations of bisphosphonate and their methods of use to treat/prevent diseases to bone remodeling or bone disorders, such as for example, Paget's disease, osteoporosis, metastatic bone disease, hypercalcemia of malignancy, periprosthetic osteolysis, periodontal disease, arthritic conditions, and the like, while minimizing the potential for esophageal irritation and other adverse gastrointestinal effects. These methods comprise orally administering to a mammal the liquid **pharmaceutical compn** . of at least 1 bisphosphonate, or a salt, as a unit dosage according to a continuous schedule having a once-weekly, twice-weekly, biweekly, twice-monthly, or monthly dosing interval. Thus, a formulation contained alendronate monosodium trihydrate 2.454, and sodium citrate dihydrate 21.18 mg/mL, NaOH and HCl qs to pH 6.8, and water qs to 1.00 mL.

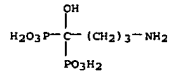
IT **66376-36-1**, Alendronate **121268-17-5**, Alendronate monosodium trihydrate **260055-05-8**, Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid bisphosphonate formulations for bone disorders)

RN **66376-36-1** HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



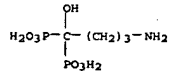
RN **121268-17-5** HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



● Na

●3 H_2O

RN **260055-05-8** HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)



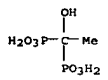
● Na

● H_2O

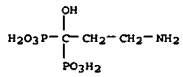
IT **2809-21-4** **40391-99-9** **89987-06-4**, Tiludronate **105462-24-6** **129318-43-0**, MonoSodium Alendronate **157432-53-6** **160982-64-9**, Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt **548457-54-1** **548457-56-3** **548457-59-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid bisphosphonate formulations for bone disorders)

RN **2809-21-4** HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

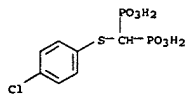
L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



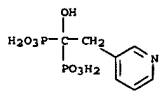
RN **40391-99-9** HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN **89987-06-4** HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



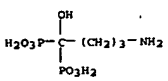
RN **105462-24-6** HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



RN **129318-43-0** HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

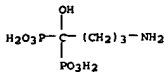
Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



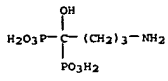
● Na

RN 157432-53-6 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, magnesium salt (9CI) (CA INDEX NAME)



●x Mg

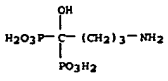
RN 160982-64-9 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt (9CI) (CA
INDEX NAME)



●x Na

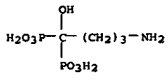
RN 548457-54-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, potassium salt (9CI) (CA INDEX NAME)

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



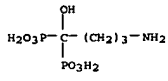
●x K

RN 548457-56-3 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (9CI) (CA INDEX NAME)



●x Ca

RN 548457-59-6 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, ammonium salt (9CI) (CA INDEX NAME)



●x NH_3

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L24 ANSWER 21 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:334829 HCAPLUS
DOCUMENT NUMBER: 138:343889
TITLE: Novel **pharmaceutical** compounds containing drugs bound to polypeptides
INVENTOR(S): Picariello, Thomas
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 4662 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034980	A2	20030501	WO 2001-US43089	20011114
WO 2003034980	C1	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2428971	AA	20030501	CA 2001-2428971	20011114
EP 1401374	A1	20040331	EP 2001-274606	20011114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

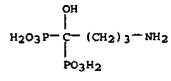
PRIORITY APPLN. INFO.:
US 2000-274622P P 20001114
US 2000-247622P P 20001114
WO 2001-US43089 W 20011114

AB **Compns.** comprising polypeptides and drugs covalently attached to the polypeptide are disclosed. Also provided is a method for delivery of these drugs to a patient comprising administering to the patient a **composition** comprising a polypeptide and a drug covalently attached to the polypeptide. Also provided is a method for protecting drugs from degradation comprising covalently attaching them to a polypeptide. Also provided is a method for **controlling release** of drugs from a **composition** comprising covalently attaching them to the polypeptide.

IT **66376-36-1DP**, Alendronate, protein conjugates
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel **pharmaceutical** compds. containing drugs bound to polypeptides)

RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 21 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:202410 HCAPLUS
DOCUMENT NUMBER: 138:226705
TITLE: Novel **pharmaceuticals** comprising drug conjugates with polypeptide carriers
INVENTOR(S): Picariello, Thomas
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 2059 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020200	A2	20030313	WO 2001-US43117	20011116
WO 2003020200	A3	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429345	AA	20030313	CA 2001-2429345	20011116
EP 1357928	A2	20031105	EP 2001-273387	20011116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2000-248600P	P 20001116
			US 2000-248601P	P 20001116
			US 2000-248603P	P 20001116
			US 2000-248604P	P 20001116
			US 2000-248606P	P 20001116
			US 2000-248607P	P 20001116
			US 2000-248608P	P 20001116
			US 2000-248609P	P 20001116
			US 2000-248611P	P 20001116
			US 2000-248689P	P 20001116
			US 2000-248691P	P 20001116
			US 2000-248692P	P 20001116
			US 2000-248693P	P 20001116
			US 2000-248694P	P 20001116

L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

US 2000-248695P	P	20001116
US 2000-248696P	P	20001116
US 2000-248697P	P	20001116
US 2000-248698P	P	20001116
US 2000-248701P	P	20001116
US 2000-248702P	P	20001116
US 2000-248703P	P	20001116
US 2000-248704P	P	20001116
US 2000-248705P	P	20001116
US 2000-248706P	P	20001116
US 2000-248707P	P	20001116
US 2000-248708P	P	20001116
US 2000-248709P	P	20001116
US 2000-248710P	P	20001116
US 2000-248711P	P	20001116
US 2000-248712P	P	20001116
US 2000-248686P	P	20001116
US 2000-248688P	P	20001116
US 2000-248714P	P	20001116
US 2000-248715P	P	20001116
US 2000-248716P	P	20001116
US 2000-248717P	P	20001116
US 2000-248718P	P	20001116
US 2000-248719P	P	20001116
US 2000-248720P	P	20001116
US 2000-248748P	P	20001116
US 2001-248664P	P	20011116
US 2001-248665P	P	20011116
US 2001-248666P	P	20011116
US 2001-248667P	P	20011116

L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

US 2001-248668P	P	20011116
US 2001-248669P	P	20011116
US 2001-248671P	P	20011116
US 2001-248672P	P	20011116
US 2001-248673P	P	20011116
US 2001-248674P	P	20011116
US 2001-248675P	P	20011116
US 2001-248676P	P	20011116
US 2001-248677P	P	20011116
US 2001-248678P	P	20011116
US 2001-248679P	P	20011116
US 2001-248680P	P	20011116
US 2001-248681P	P	20011116
US 2001-248682P	P	20011116
US 2001-248683P	P	20011116
US 2001-248684P	P	20011116
US 2001-248765P	P	20011116
US 2001-248766P	P	20011116
US 2001-248767P	P	20011116
US 2001-248773P	P	20011116
US 2001-248774P	P	20011116
US 2001-248775P	P	20011116
US 2001-248778P	P	20011116
US 2001-248780P	P	20011116
US 2001-248781P	P	20011116
US 2001-248783P	P	20011116
US 2001-248784P	P	20011116
US 2001-248785P	P	20011116
US 2001-248786P	P	20011116
US 2001-248787P	P	20011116

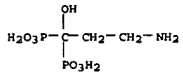
L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

US 2001-248790P	P	20011116
US 2001-248791P	P	20011116
US 2001-248792P	P	20011116
US 2001-248793P	P	20011116
US 2001-248833P	P	20011116
US 2001-248848P	P	20011116
US 2001-248849P	P	20011116
WO 2001-US43117	W	20011116

AB A **pharmaceutical composition** comprising a polypeptide and an active agent attached to said polypeptide is disclosed.

IT 40391-99-9D, polypeptide conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **pharmaceuticals** comprising drug conjugates with polypeptide carriers)

RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



Searched by: Mary Hale 571-272-2507 REM 1D86

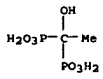
L24 ANSWER 23 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:154278 HCAPLUS
DOCUMENT NUMBER: 138:198670
TITLE: GnRh agonist combination drugs
INVENTOR(S): Furuya, Shuichi; Kusaka, Masami
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015820	A1	20030227	WO 2002-JP8130	20020808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003137814	A2	20030514	JP 2002-231922	20020808
EP 1424080	A1	20040602	EP 2002-758814	20020808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			JP 2001-244616	A 20010810
			WO 2002-JP8130	W 20020808

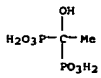
AB In the field of **pharmaceuticals**, it is intended to provide drugs whereby the preventive and therapeutic effects of a GnRH agonist on various diseases can be enhanced and QOL can be improved. More specifically, combination drugs characterized in that the GnRH agonist is combined with a chemical selected from among SERM, SARM, sex hormone synthesis inhibitors, receptor-type tyrosine kinase inhibitors, bone metabolism regulators, drugs for immunotherapy, cytokine/chemokine inhibitors and endothelin receptor antagonists. Owing to these combinations, excellent effects of enhancing the preventive and therapeutic effects of the GnRH agonist on various diseases and relieving side effects can be established. Furthermore, QOL can be improved thereby.

IT **2809-21-4**, Etidronic acid **40391-99-9**, Pamidronic acid **66376-36-1**, Alendronic acid **105462-24-6**, Risedronic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH agonist combination drugs for treating various diseases and relieving side effects)

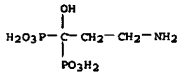
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



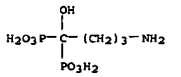
L24 ANSWER 23 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



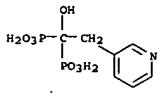
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 24 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:76580 HCAPLUS
DOCUMENT NUMBER: 138:126974
TITLE: Dosage forms for immediate gastric release of a calcium transport stimulator coupled with delayed gastric release of a bis-phosphonate
INVENTOR(S): Fleshner-Barak, Moshe
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007916	A1	20030130	WO 2002-US22825	20020717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1416919	A1	20040512	EP 2002-750134	20020717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-305913P	P 20010717
			WO 2002-US22825	W 20020717

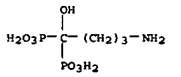
AB The present invention provides a gastric retention dosage form for immediate or uncontrolled release of a vitamin D derivative that stimulates calcium absorption from the intestine, like calcitriol, alphacalcidol and calcifediol, combined with delayed release of a bis-phosphonate calcium resorption inhibitor such as alendronic acid and its **pharmaceutically** acceptable salts and hydrates.

IT **2809-21-4** **66376-36-1**, Alendronic acid **89987-06-4**, Tiludronate **105462-24-6** **121268-17-5** **260055-05-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosage forms for immediate gastric release of calcium transport stimulator coupled with delayed gastric release of bis-phosphonate)

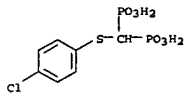
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 24 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

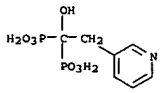
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



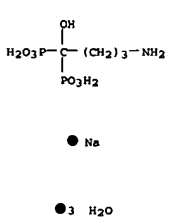
RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



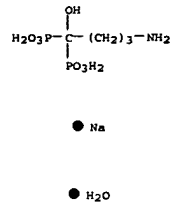
RN 121268-17-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 24 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 260055-05-8 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)



● Na

● H_2O

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L24 ANSWER 25 OF 79 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:64836 BIOSIS
DOCUMENT NUMBER: PREV200400065894
TITLE: Preparation of 1-hydroxyethylidene-1,1-diphosphonic acid-intercalated layered double hydroxide and its physicochemical properties.
AUTHOR(S): Nakayama, Hirokazu [Reprint Author]; Takeshita, Koji; Tsuhako, Mitsutomo
CORPORATE SOURCE: Department of Functional Molecular Chemistry, Kobe Pharmaceutical University, 4-19-1 Motoyamakitamachi, Higashinada-ku, Kobe, 658-8558, Japan
hiro@kobepharma-u.ac.jp
SOURCE: Journal of Pharmaceutical Sciences, (December 2003) Vol. 92, No. 12, pp. 2419-2426. print.
CODEN: JPMSAE. ISSN: 0022-3549.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jan 2004
Last Updated on STN: 28 Jan 2004

AB The intercalation of 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP), which is a drug for osteoporosis, in layered double hydroxide (LDH) was examined with the goal of developing a novel drug delivery system (DDS) of
HEDP. To prevent side reactions, the intercalation reaction was carried out at 0degreeC, and at pH 4-6. The uptake of HEDP was determined as 3.5 mmol g-1 of LDH, and the interlayer distance increased from 7.8 to 13 ANG.
The HEDP-release profiles into K2CO3 aqueous solution and into various buffer solutions were also examined.

L24 ANSWER 26 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003432402 EMBASE
TITLE: Drug-Induced Esophageal Injuries and Dysphagia.
AUTHOR: O'Neill J.L.; Remington T.L.
CORPORATE SOURCE: T.L. Remington, University of Michigan Health System, Department of Pharmacy UH B2 D301, 1500 E. Medical Center Dr., Ann Arbor, MI 48109-0008, United States.
remingtn@umich.edu
SOURCE: Annals of Pharmacotherapy, (2003) 37/11 (1675-1684).
Refs: 110
ISSN: 1060-0280 CODEN: APHRER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English; Spanish; French

AB OBJECTIVE: To review and analyze medical literature documenting drug-induced esophageal injury and dysphagia and to formulate strategies to enhance **pharmacists'** prevention, detection, and treatment of these iatrogenic complications. DATA SOURCES: A MEDLINE search (1966-April
2002) was conducted to identify primary and secondary literature using variable combinations of the following search terms: pill-induced, drug-induced, or iatrogenic with esophageal injury, esophageal damage, or dysphagia. Bibliographies were also reviewed to identify additional relevant references. STUDY SELECTION AND DATA EXTRACTION: All case reports, reviews, and clinical studies relating to drug-induced esophageal
injury or swallowing dysfunction were evaluated. DATA SYNTHESIS: Drug-induced esophageal injury may be under-recognized. Several drugs have
been associated with physical or chemically mediated injuries. Risk factors for injury have been identified and preventive and treatment strategies have been successful in limiting esophageal injury. Drug-induced dysphagia can have serious complications and is most often associated with typical neuroleptics such as haloperidol. CONCLUSIONS: **Pharmacists** can play a pivotal role in proactively identifying situations where there is a higher likelihood of drug-induced esophageal injury or dysphagia. They can recommend preventive strategies to promote safe medication use, help identify iatrogenic complications when they occur, and assist in formulation of appropriate treatment strategies.

L24 ANSWER 27 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

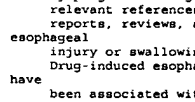
ACCESSION NUMBER: 2003:383077 HCAPLUS
DOCUMENT NUMBER: 140:117159
TITLE: Oral **pharmaceutical** formulations for bone resorption inhibitor
AUTHOR(S): Anon.
CORPORATE SOURCE: UK
SOURCE: Research Disclosure (2003), 468(April), PS23 (No. 467143)
CODEN: RSDSBB; ISSN: 0374-4353
PUBLISHER: Kenneth Mason Publications Ltd.
DOCUMENT TYPE: Journal; Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RD 467143		20030310		
PRIORITY APPLN. INFO.:			RD 2003-467143	20030310

AB The chemical formula is presented of an active ingredient in oral formulations for bone resorption inhibitor. Ingredients and dosage forms of the formulation are described.

IT **66376-36-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **pharmaceutical** formulations for bone resorption inhibitor)

RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 28 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2004037637 EMBASE
TITLE: A case history illustrating how extended release cholinesterase inhibitors could improve management of Alzheimer's disease [1].
AUTHOR: Alisky J.M.
CORPORATE SOURCE: J.M. Alisky, Marshfield Clin. Research Foundation, Marshfield Clinic-Thorp Center, 1000 Oak Avenue, Marshfield, WI 54449, United States. Alisky.Joseph@marshfieldclinic.org
SOURCE: Journal of Alzheimer's Disease, (2003) 5/6 (477-478). ISSN: 1387-2877 CODEN: JADIF
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English

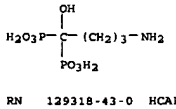
L24 ANSWER 29 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003440086 EMBASE
TITLE: Polyphosphates and Other Phosphorus-Containing Polymers for Drug Delivery Applications.
AUTHOR: Chaubal M.V.; Gupta A.S.; Lopina S.T.; Bruley D.F.
CORPORATE SOURCE: M.V. Chaubal, Baxter Healthcare, Route 120 and Wilson Road, Round Lake, IL 60073, United States
SOURCE: Critical Reviews in Therapeutic Drug Carrier Systems, (2003) 20/4 (295-315). Refs: 62 ISSN: 0743-4863 CODEN: CRTSEO
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Poly(phosphate ester)s, polyphosphonates, and polyphosphazenes are three classes of phosphorus-containing polymers that have received wide attention over the past decade for their utility in biomedicine and tissue engineering. These three families of polymers can lead to a number of subclasses of polymers with varied properties. Significant research in this area has led to niche polymers with morphologies ranging from viscous gels to amorphous microparticles for utility in drug delivery. Furthermore, the pentavalency of phosphorus offers the potential for covalent linking of the drug. The classes of polymers discussed in this review are being explored in human clinical trials for vaccine delivery as well as delivery of oncolytic and CNS therapeutics. More applications in the areas of DNA delivery and tissue engineering are also being explored.

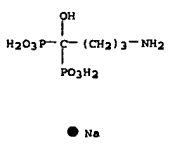
L24 ANSWER 30 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:486649 HCAPLUS
DOCUMENT NUMBER: 140:258856
TITLE: Oral **pharmaceutical** formulations for bone resorption inhibitor
AUTHOR(S): Anon.
CORPORATE SOURCE: USA
SOURCE: IP.com Journal (2003), 3(4), 61 (No. IPCOM000011782D)
, 14 Mar 2003
CODEN: IJPOBX; ISSN: 1533-0001
PUBLISHER: IP.com, Inc.
DOCUMENT TYPE: Journal; Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IP 11782D		20030314		
PRIORITY APPLN. INFO.:			IP 2003-11782D	20030314

AB **Sustained, controlled** or immediate **release** oral dosage forms capable of releasing the active **pharmaceutical** ingredient, optionally in the form of its monosodium salt trihydrate, to human patients immediately or over extended periods following administration are reported.
IT **66376-36-1 129318-43-0**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **pharmaceutical** formulations for bone resorption inhibitor)
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

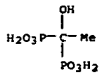


L24 ANSWER 31 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:813899 HCAPLUS
DOCUMENT NUMBER: 137:299972
TITLE: Modification of the **sustained-release** profile of a drug by a biocompatible polymer and a bisphosphonate
INVENTOR(S): Dasch, James R.; Riley, M. Gary I.
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

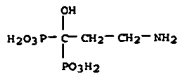
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083096	A1	20021024	WO 2002-US8440	20020319
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004100	A1	20030102	US 2001-835001	20010413
US 6558702	B2	20030506		
CA 2444421	AA	20021024	CA 2002-2444421	20020319
EP 1395240	A1	20040310	EP 2002-709857	20020319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532218	T2	20041021	JP 2002-580900	20020319
US 2003236192	A1	20031225	US 2003-400162	20030325
US 2004147488	A1	20040729	US 2004-758717	20040116
PRIORITY APPLN. INFO.:			US 2001-835001 A	20010413
			WO 2002-US8440 W	20020319
			US 2003-400162 A1	20030325

AB The present invention relates to a method for the **sustained release** in vivo of a biol. active agent comprising administering to a subject in need of treatment an effective amount of a **sustained-release composition** comprising a biocompatible polymer having the biol. active agent incorporated therein, and a bisphosphonate wherein the bisphosphonate compound is present in an amount sufficient to modify the release profile of the biol. active agent from the **sustained-release composition**
Pharmaceutical compns. suitable for use in the method of the invention are also disclosed.
IT **2809-21-4 57248-88-1 66376-36-1**, Alendronate **89987-06-4**, Tiludronate **115436-72-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modification of **sustained-release** profile of drug by biocompatible polymer and bisphosphonate)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 31 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

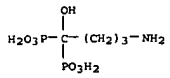


RN 57248-88-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

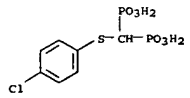


●2 Na

RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

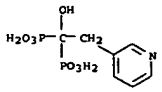


RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 115436-72-1 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 31 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 32 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:615414 HCAPLUS
DOCUMENT NUMBER: 137:159355
TITLE: **Compositions** containing bisphosphonates for management of bone density
INVENTOR(S): Chan, Tai Wah
PATENT ASSIGNEE(S): Durect Corporation, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

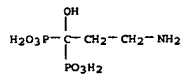
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062352	A2	20020815	WO 2002-US3794	20020207
WO 2002062352	A3	20030403		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2438208	AA	20020815	CA 2002-2438208	20020207
US 2002151876	A1	20021017	US 2002-71821	20020207
EP 1365770	A2	20031203	EP 2002-718929	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2001-267323P	P 20010207
			WO 2002-US3794	W 20020207

AB The invention features devices and methods for the delivery of a formulation to an individual to stabilize or increase bone mass by increasing bone deposition and/or decreasing bone resorption. In the present invention, a drug formulation comprising a bisphosphonate is provided parenterally in a **sustained release** dosage form, e.g., as an injected matrix or stored within a drug delivery device.
In a specific embodiment, the dosage form may be implanted or injected into a site in the body (i.e., implantation site) and a conduit, e.g., a catheter, can be used to transport the formulation from the dosage form for release at a site in the body distal form the implantation site. Pamidronate sodium was reconstituted with 10 mL phosphate buffered saline to achieve a concentration of 9 mg/mL. The 9 mg/mL solution was then diluted to achieve a concentration of 0.9 mg/mL.

IT 57248-88-1, Disodium Pamidronate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns.** containing bisphosphonates for management of bone d.)

RN 57248-88-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 32 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●2 Na

L24 ANSWER 33 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:555334 HCAPLUS
DOCUMENT NUMBER: 137:114525
TITLE: Syntactic deformable **pharmaceutical** foam **compositions**
INVENTOR(S): Odidi, Isa; Odidi, Amina
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

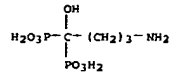
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002056861	A2	20020725	WO 2002-CA54		20020117
WO 2002056861	A3	20021017			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 6800668	B1	20041005	US 2001-765783		20010119
CA 2435276	AA	20020725	CA 2002-2435276		20020117
PRIORITY APPLN. INFO.:			US 2001-765783	A	20010119
			WO 2002-CA54	W	20020117

AB The invention relates to methods for preparing a syntactic foam compn. suitable for use as a carrier for chems. or other compds., including **pharmaceuticals**. Carbopol 971P, hydroxyethyl cellulose, cellulose microspheres and silica, was mixed in a high-shear mixer. The resulting admixt. was treated with 2-propanol, while simultaneously subjecting the admixt. to high-shear forces in the high-shear mixer. This mixing created a uniform stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying. Metoprolol succinate was added to the above admixt. and subjected to high-shear agitation for 2 min before treatment with 2-propanol. A stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying was obtained. This was dried at 40°. The dried foam was the disentangled by size reduction to obtain discrete particles. The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an aqueous medium, released metoprolol over a period of ≤3 h.

IT **66376-36-1**, Alendronate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syntactic deformable **pharmaceutical** foam **compns.**)

RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 33 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 34 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:107047 HCAPLUS
DOCUMENT NUMBER: 136:156434
TITLE: Vaginal delivery of bisphosphonates
INVENTOR(S): Harrison, Donald C.; Liu, James H.
PATENT ASSIGNEE(S): UMD, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

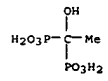
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002009631	A1	20020207	WO 2001-US22205		20010712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6572874	B1	20030603	US 2000-626025		20000727
AU 765269	B2	20030911	AU 2001-54192		20010703
EP 1311213	A1	20030521	EP 2001-957150		20010712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001013134	A	20040622	BR 2001-13134		20010712
JP 2004519420	T2	20040702	JP 2002-515186		20010712
NO 2003000422	A	20030311	NO 2003-422		20030127
PRIORITY APPLN. INFO.:			US 2000-626025	A	20000727
			US 1998-79897	A2	19980515
			AU 1998-76976	A3	19980610
			US 1999-146218P	P	19990728
			WO 2001-US22205	W	20010712

AB A targeted site delivery of bisphosphonates to the vagina using a medicated intravaginal device comprising a bisphosphonate **composition** formulated for transvaginal delivery is described. A method for **treatment** of osteoporosis and related bone and skeleton diseases, for prevention of bone breakdown and loss of bone mass and strength by intravaginal administration of bisphosphonates to the vagina and transvaginal delivery of bisphosphonates to the general circulation. For example, vaginal suppositories were prepared containing alendronate (14 mg/kg body weight) using Suppocire AS2 (75%), hydroxypropyl Me cellulose (10%), as a mucoadhesive agent, and Transcutol (15%), as a penetration enhancer.

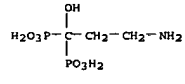
IT **2809-21-4** **40391-99-9** **66376-36-1**, Alendronate
89987-06-4, Tiludronate **105462-24-6**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaginal delivery of bisphosphonates for treatment of osteoporosis and related bone diseases)

L24 ANSWER 34 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

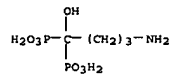
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



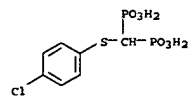
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

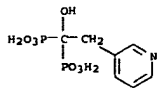


RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

L24 ANSWER 34 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

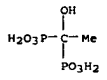


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

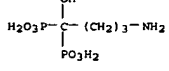
FORMAT

L24 ANSWER 35 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
study); USES (Uses)
(**pharmaceutical compns.** having improved peroral absorbability contg. drugs, aminoalkylmethacrylate copolymer E, and acids)

RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L24 ANSWER 35 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:71846 HCAPLUS
DOCUMENT NUMBER: 136:123663
TITLE: **Pharmaceutical composition** improved in peroral absorbability
INVENTOR(S): Watanabe, Shunsuke; Takemura, Shigeo; Tsutsui, Yuuki; Kondo, Hiromu; Nakanishi, Kiyo; Sako, Kazuhiro; Sawada, Toyohiro
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005786	A1	20020124	WO 2001-JP6135	20010716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2415643	AA	20020124	CA 2001-2415643	20010716
US 2002150624	A1	20021017	US 2001-907557	20010716
EP 1302201	A1	20030416	EP 2001-949994	20010716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 3563070	B2	20040908	JP 2002-511719	20010716
JP 2004083601	A2	20040318	JP 2003-419042	20031217

PRIORITY APPLN. INFO.:
US 2000-218980P P 20000717
JP 2002-511719 A3 20010716
WO 2001-JP6135 W 20010716

AB Disclosed is a **pharmaceutical composition** improved in peroral absorbability, which comprises a drug, aminoalkyl methacrylate copolymer E, and an acid substance and in which the three components stand adjacent to each another and at least the copolymer and the acid substance are uniformly dispersed; a method for improving peroral absorbability by using the **composition**; and a peroral absorption improver for enhancing the penetration of drug into the gastrointestinal mucosa and/or the mucous blanket present on the surface thereof, which contains aminoalkyl methacrylate copolymer E as the active ingredient. A powder was prepared by mixing and drying of Bu methacrylate-dimethylaminoethyl methacrylate-Me methacrylate copolymer (Eudragit E100)/Tween 80 (10:1) 1650 and 1 M HCl/ethanol (5:12) 12000 g. The obtained powder 125 mg was combined with [1-Hydroxy-2-imidazo-(1,2-a)pyridin-3-ylethylidene]bis-phosphonate 10 and lactose 65 mg to obtain a tablet showing improved Cmax and AUC values in dog.

IT **2809-21-4 66376-36-1**, Alendronate
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological

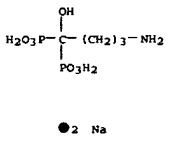
L24 ANSWER 36 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:10272 HCAPLUS
DOCUMENT NUMBER: 136:74650
TITLE: Rapidly expanding **composition** for gastric retention and **controlled release** of therapeutic agents
INVENTOR(S): Fleshner-Barak, Moshe; Lerner, E. Itzhak; Rosenberger, Vered; Dahan, Mazal; Imakov, Yisrael
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

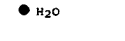
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000213	A1	20020103	WO 2001-US20134	20010622
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412490	AA	20020103	CA 2001-2412490	20010622
EP 1305021	A1	20030502	EP 2001-946709	20010622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501190	T2	20040115	JP 2002-504995	20010622
US 2003203878	A1	20031030	US 2003-420403	20030422

PRIORITY APPLN. INFO.:
US 2000-213832P P 20000623
US 2000-217110P P 20000710
US 2000-223212P P 20000804
US 2001-260438P P 20010109
US 2001-770898 A1 20010126
WO 2001-US20134 W 20010622
US 2002-246502 B1 20020916

AB The present invention provides a **pharmaceutical composition** for use in a dosage form for oral administration to a patient. The **composition** expands upon contact with gastric fluid and promotes retention of the dosage form in the patient's stomach for a prolonged period of time. The present invention further provides **pharmaceutical** dosage forms containing an active ingredient, and the **pharmaceutical composition** The forms are adapted for immediate or **controlled release** of the active ingredient. The dosage forms may be used advantageously in the treatment of Parkinson's disease with levodopa and hyperactivity and attention

L24 ANSWER 36 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
deficit disorder with methylphenidate. A tablet contained sodium alendronate monohydrate 1.67, hydroxypropyl Me cellulose 16.7, hydroxypropyl cellulose 56.6, croscarmellose sodium 14, tannic acid 10, and magnesium stearate 1%. The cumulative realest of alendronate from the
tablet after 24 h was 45%.
IT 185959-98-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapidly expanding composition for gastric retention and controlled release of therapeutic agents)
RN 185959-98-2 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)





REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:10265 HCAPLUS
DOCUMENT NUMBER: 136:74647
TITLE: Composition and dosage form for delayed gastric release of alendronate and/or other bis-phosphonates
INVENTOR(S): Flashner-Barak, Moshe; Rosenberger, Vered; Dahan, Mazal; Lerner, Yitzhak
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

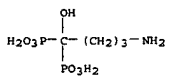
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000204	A1	20020103	WO 2001-US20130	20010622
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002015733	A1	20020207	US 2001-770898	20010126
US 6476006	B2	20021105		
CA 2412024	AA	20020103	CA 2001-2412024	20010622
EP 1296657	A1	20030402	EP 2001-946706	20010622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501186	T2	20040115	JP 2002-504986	20010622
US 2003203878	A1	20031030	US 2003-420403	20030422

PRIORITY APPLN. INFO.:

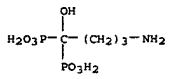
US 2000-213832P	P	20000623
US 2001-260438P	P	20010109
US 2001-770898	A	20010126
WO 2001-US20130	W	20010622
US 2002-246502	B1	20020916

AB The present invention provides compacted **pharmaceutical compns.** for oral administration to a patient which expands upon contact with gastric fluid to retain a dosage form in the patient's stomach for an extended period of time, the formulation comprising a non-hydrated hydrogel, a superdisintegrant and tannic acid. The present invention further provides a **pharmaceutical** dosage form containing an active ingredient, and the compacted **pharmaceutical composition** The invention further provides a dosage form suitable for delivering a therapeutic bisphosphonate such as alendronate to the stomach
of a patient over an extended period. Thus, an extended-release tablet formulation contained HPMC 15.9, hydroxypropyl cellulose 47.6, sodium starch glycolate 31.7, and tannic acid 4.8%. Sodium alendronate

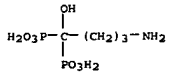
L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
formulated in another tablet formulation was incorporated into the above tablet formulation. The tablets obtained had good mech. strength.
IT **66376-36-1**, Alendronic acid **66376-36-1D**, Alendronic acid, salts **121268-17-5 260055-05-8 385396-33-8**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosage forms for delayed gastric release of alendronate and/or other bisphosphonates)
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

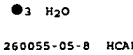


RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



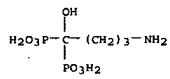
RN 121268-17-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



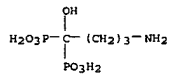


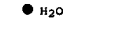
RN 260055-05-8 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)

L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

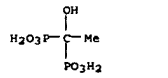


RN 385396-33-8 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt, monohydrate (9CI) (CA INDEX NAME)



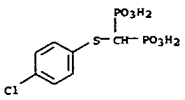


IT **2809-21-4 89987-06-4**, Tiludronate **105462-24-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosage forms for delayed gastric release of alendronate and/or other bisphosphonates)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

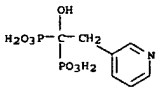


RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)

L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



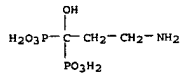
RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



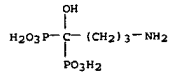
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

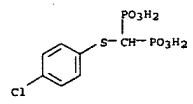
L24 ANSWER 38 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



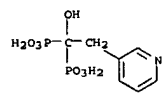
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 38 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

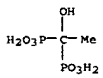
ACCESSION NUMBER: 2004:951507 HCAPLUS
DOCUMENT NUMBER: 142:246092
TITLE: Implantable **sustained release** formulation of bisphosphonate bone resorption inhibitor
INVENTOR(S): Kang, Gil Seon; Kim, Hyeong Jong; Kim, Sang Uk; Lee, Hae Bang; Lee, Jeong Sik; Sung, Ha Su
PATENT ASSIGNEE(S): Korea Research Institute of Chemical Technology, S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2002080018	A	20021023	KR 2001-19043	20010410
PRIORITY APPLN. INFO.:			KR 2001-19043	20010410

AB A **sustained release** formulation obtained by inclusion of bisphosphonate as an inhibitor of bone resorption into a biodegradable polymer and formulation thereof into an implant type is provided which can be administered to the effected part of a patient suffering from bone disease by injection or operation, etc. This **sustained release** formulation comprises 0.01 to 70% by weight of a bisphosphonate based bone resorption inhibitor and 30 to 99.99% by weight of a biodegradable polymer and is in the shape of 0.1 μ to 20mm fine particles, microsphere, microcapsule, fine powder and paste. The bisphosphonate based bone resorption is one or more selected from Etidronate, Clodronate, Tiludronate, Pamidronate, Alendronate, Risedronate, Ibandronate, Zolendronate and a **pharmaceutically** acceptable salt, hydrate and a partial hydrate thereof.

IT **2809-21-4 40391-99-9 66376-36-1**, Alendronate **89987-06-4**, Tiludronate **105462-24-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable **sustained release** formulation of bisphosphonate bone resorption inhibitor)

RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 39 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

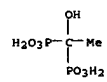
ACCESSION NUMBER: 2002:693116 HCAPLUS
DOCUMENT NUMBER: 137:222060
TITLE: Method for manufacture of **pharmaceutical** granules
INVENTOR(S): Ochiai, Yasushi; Wakisaka, Kouji
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238662	A2	20020911	EP 2002-5224	20020307
EP 1238662	A3	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002332226	A2	20021122	JP 2002-61478	20020307
US 2003039699	A1	20030227	US 2002-91559	20020307
PRIORITY APPLN. INFO.:			JP 2001-64056 A	20010307

AB Coated **pharmaceutical** granules contain a water-soluble drug as an active ingredient at a high d., which is superior in uniform content and stability, and which is capable of providing a **pharmaceutical** formulation superior in drug **release control** and having a smaller size than conventional prepns., and a production method for the manufacture of granules. Ny using a rotary fluidized-bed granulation apparatus, an aqueous solution of metformin-HCl was sprayed on single crystals of the drug charged in the apparatus The granules were dried, and after drying, the granules were sieved to give granules with a particle size of 500-840 μm.

IT **7414-83-7**, Sodium ethidronate
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method for manufacture of **pharmaceutical** granules)

RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L24 ANSWER 39 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

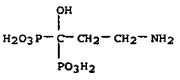
L24 ANSWER 40 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:782875 HCAPLUS
DOCUMENT NUMBER: 138:326440
TITLE: Preparation and characterization of pamidronate-loaded PLGA wafer for the treatment of bone resorption
AUTHOR(S): Yoo, Je-Young; Kim, Sang Wook; Khang, Gilson; Seong, Ha Soo; Jeong, Je Kyo; Kim, Hyung Jong; Lee, Jung Sik; Lee, Hai Bang
CORPORATE SOURCE: Dept. of Advanced Organic Materials Eng., Chonbuk National Univ., Jeonju, 561-756, S. Korea
SOURCE: Polymer (Korea) (2002), 26(5), 680-690
CODEN: POLLDG; ISSN: 0379-153X
PUBLISHER: Polymer Society of Korea
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB Implantable biodegradable wafers were prepared with pamidronate-loaded poly(L-lactide-co-glycolide) (PLGA, 75:25 mol ratio by lactide to glycolide, mol. weight; 20000 and 90000 g/mol) by direct compression method for the **sustained release** of pamidronate to investigate the possibility for the treatment of bone resorption. Pamidronate-loaded PLGA powders were prepared by means of phys. mixing and spray drying with the control of formulation factors and characterized by scanning electron microscope and X-ray diffractometer. The pamidronate-loaded PLGA powders fabricated into wafers by direct compression under the constant pressure and time at room temperature These wafers were also observed for their structural characteristic, release pattern, and degradation pattern. The release rate of pamidronate increased with increasing their initial loading ratio as well as increasing wafer thickness. The mol. weight of PLGA affects the release pattern: the higher mol. weight of PLGA, the faster release rate. It can be explained that the higher viscosity of high mol. PLGA solution at same concentration tends to aggregate PLGA and pamidronate resulting in unstable **pharmaceutical** dosage form. This system had advantages in terms of simplicity in design and obviousness of drug release rate and may be useful as an implantable dosage form for the treatment of aural cholesteatoma.

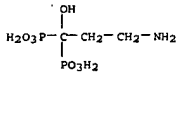
IT **40391-99-9 57248-88-1**, Pamidronate disodium
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and characterization of pamidronate-loaded PLGA wafer for treatment of bone resorption)

RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 40 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 57248-88-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L24 ANSWER 41 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002163708 EMBASE
TITLE: Venlafaxine-associated vaginal bleeding.
AUTHOR: Linnebur S.A.; Saseen J.J.; Pace W.D.
CORPORATE SOURCE: S.A. Linnebur, Univ. of Colorado Hlth. Sci. Center, Department of Pharmacy Practice, School of Pharmacy, 4200 East Ninth Avenue, Denver, CO 80262, United States. sunny.linnebur@uchsc.edu
SOURCE: Pharmacotherapy, (2002) 22/5 (652-655).
Refs: 10
ISSN: 0277-0008 CODEN: PHPYDQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A 41-year-old amenorrheic woman started taking venlafaxine 37.5 mg/day for treatment of depression; 7 days later, she experienced vaginal bleeding, which ceased 1 day after she stopped taking the drug. On rechallenge with venlafaxine, she again experienced vaginal bleeding that resolved after discontinuation. We found no published reports describing vaginal bleeding associated with venlafaxine. However, premarketing and postmarketing data report similar adverse effects in patients taking the agent. In addition, several cases of menstrual irregularities have occurred with two other anti-depressants: fluoxetine and bupropion. This case report supports previous surveillance data indicating that venlafaxine may cause vaginal bleeding.

Searched by: Mary Hale 571-272-2507 REM 1D86

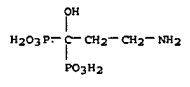
L24 ANSWER 42 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2002437234 EMBASE
TITLE: Analgesia issues in palliative care: Bone pain, **controlled release** opioids, managing opioid-induced constipation and nifedipine as an analgesic.
AUTHOR: Fine P.G.
CORPORATE SOURCE: Dr. P.G. Fine, Department of Anesthesiology, School of Medicine, University of Utah, 50 North Medical Drive, Salt Lake City, UT 84132, United States. fine@arcs.net
SOURCE: Journal of Pain and Palliative Care Pharmacotherapy, (2002)
16/1 (93-97).
Refs: 4
ISSN: 1536-0288 CODEN: JPPCBG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Some recent literature relevant to analgesia in palliative care is reviewed. Reports on clinical use of bisphosphonates for bone pain in cancer, **controlled release** opioids, selection of laxatives for opioid-induced constipation and the calcium channel blocker nifedipine as an analgesic are described. .COPYRGT. 2002 by The Haworth Press, Inc. All rights reserved.

L24 ANSWER 43 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:833023 HCAPLUS
DOCUMENT NUMBER: 135:376738
TITLE: Compounds and methods for modulating cerebral amyloid angiopathy using inhibitors of an amyloid β peptide
INVENTOR(S): Green, Allan M.; Gervais, Francine
PATENT ASSIGNEE(S): Neurochem, Inc., Can.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

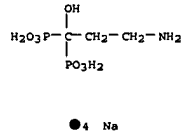
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085093	A2	20011115	WO 2000-IB2078	20001222
WO 2001085093	A3	20020829		
WO 2001085093	C2	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395314	AA	20011115	CA 2000-2395314	20001222
AU 2001084313	A5	20011120	AU 2001-84313	20001222
EP 1251837	A2	20021030	EP 2000-993855	20001222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000016652	A	20021119	BR 2000-16652	20001222
US 2003003141	A1	20030102	US 2000-747408	20001222
US 6670399	B2	20031230		
JP 2003532656	T2	20031105	JP 2001-581748	20001222
PRIORITY APPLN. INFO.:			US 1999-171877P	P 19991223
			WO 2000-IB2078	W 20001222

OTHER SOURCE(S): MARPAT 135:376738
AB The invention provides methods of inhibiting cerebral amyloid angiopathy (CAA) and treating a disease state characterized by cerebral amyloid angiopathy, e.g., Alzheimer's disease, in a subject using an inhibitor of the 39-40 amino acid amyloid β peptide (Aβ40). The Aβ40 inhibitor is selected from, e.g., sulfonic acid derivs., such as ethanesulfonic acid, 1,2-ethanedisulfonic acid, 1-propanesulfonic acid, 1,3-propanedisulfonic acid, 1,4-butanedisulfonic acid, 1,5-pentanedisulfonic acid, 2-aminoethanesulfonic acid, 4-hydroxy-1-butanesulfonic acid, 1-butanesulfonic acid, 1-decanesulfonic acid, 2-propanesulfonic acid, 3-pentanesulfonic acid, 4-heptanesulfonic acid, etc., and **pharmaceutically** acceptable salts thereof or from from phosphonic acid derivs., such as diethylphosphonoacetic acid, phenylphosphonic acid, 3-aminopropylphosphonic acid, propylphosphonic acid, etc. The compds. are formulated in a dispersion system, a liposome formulation, or microspheres using a polymeric matrix. The polymeric matrix is selected from natural polymers, such as albumin, alginate, cellulose derivs., collagen, fibrin, gelatin, and polysaccharides, or

L24 ANSWER 43 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
synthetic polymers such as polyesters, polyethylene glycol, poloxamers, and polyanhydrides. For example, the ability of compds. of the invention to inhibit CAA was measured in 9 wk old hAPP transgenic mice treated with two different concns. of a compd. of the present invention, 3-amino-1-propanesulfonic acid sodium salt, 100 and 30 mg/kg. Mice were administered the compd. for 8 wk, after which they were sacrificed and their brains were perfused and processed for histol. staining with Thioflavin S. This method may also be used as a screening method for detg. activity of a candidate compd. for inhibiting CAA. The extent of CAA in brain sections obtained from these animals was qual. detd. following staining. The results indicate that the test compd. was effective in (i) reducing the no. of mice showing CAA, and (ii) showing an effect on the severity of the deposition seen in the brain vasculature of these animals.
IT **40391-99-9 91357-22-1 129318-43-0**
373645-11-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(inhibitors of amyloid β peptide for modulating cerebral amyloid angiopathy)
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

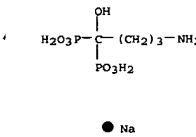


RN 91357-22-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, tetrasodium salt (9CI) (CA INDEX NAME)



RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 43 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



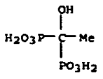
RN 373645-11-5 HCAPLUS
CN Phosphonic acid, (3-aminopropylidene)bis-, tetrasodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 44 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:780683 HCAPLUS
DOCUMENT NUMBER: 135:335156
TITLE: Modified-release formulations containing a hypnotic agent
INVENTOR(S): Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria
PATENT ASSIGNEE(S): Synthon B.V., Neth.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078725	A2	20011025	WO 2001-NL299	20010412
WO 2001078725	A3	20011220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001050661	A5	20011030	AU 2001-50661	20010412
EP 1272181	A2	20030108	EP 2001-923989	20010412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003054041	A1	20030320	US 2001-833662	20010413
US 6638535	B2	20031028		
US 2004047908	A1	20040311	US 2003-657075	20030909
PRIORITY APPLN. INFO.:			US 2000-196939P	P 20000413
			WO 2001-NL299	W 20010412
			US 2001-833662	A3 20010413

AB Hypnotic **pharmaceutical compns.** are made from pellets and exhibit a modified release. Zolpidem or a **pharmaceutically** acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a **release** rate **controlling** excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any **pharmaceutically** active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

L24 ANSWER 44 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
IT **2809-21-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified-release formulations containing hypnotic agent)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

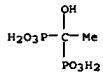


L24 ANSWER 45 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:396644 HCAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: Solid carriers for improved delivery of active ingredients in **pharmaceutical compositions**
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

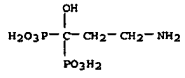
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248363	B1	20010619	US 1999-447690	19991123
CA 2391923	AA	20010531	CA 2000-2391923	20001122
EP 1233756	A1	20020828	EP 2000-980761	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T2	20030527	JP 2001-539423	20001122
PRIORITY APPLN. INFO.:			US 1999-447690	A 19991123
			WO 2000-US32255	W 20001122

AB The present invention provides solid **pharmaceutical compns.** for improved delivery of a wide variety of **pharmaceutical** active ingredients contained therein or sep. administered. In one embodiment, the solid **pharmaceutical composition** includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of **pharmaceutical** active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid **pharmaceutical composition** includes a solid carrier, the solid carrier being formed of different combinations of **pharmaceutical** active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The **compns.** of the present invention can be used for improved delivery of hydrophilic or hydrophobic **pharmaceutical** active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A **composition** contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g.
IT **7414-83-7**, Disodium etidronate **57248-88-1**, Pamidronate disodium **66376-36-1**, Alendronate **89987-06-4**, Tiludronate **105462-24-6**, Risedronic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients in **pharmaceutical compns.**)

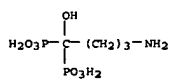
L24 ANSWER 45 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



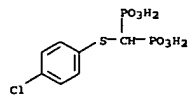
RN 57248-88-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

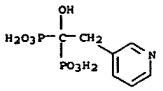


RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS

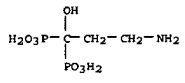
L24 ANSWER 45 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN Phosphonic acid, (1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



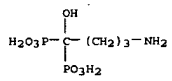
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

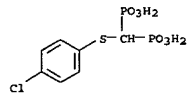
L24 ANSWER 46 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



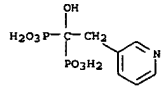
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L24 ANSWER 46 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:265229 HCAPLUS
DOCUMENT NUMBER: 134:285588
TITLE: **Pharmaceutical** formulation for menopausal women comprising fatty acids, calcium compounds, and folic acid
INVENTOR(S): Levinson, R. Saul; Hermelin, Marc S.; Kirschner, Mitchell I.
PATENT ASSIGNEE(S): KV Pharmaceutical Company, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024772	A1	20010412	WO 2000-US23527	20000828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6479545	B1	20021112	US 1999-409059	19990930
CA 2385854	AA	20010412	CA 2000-2385854	20000828
EP 1216024	A1	20020626	EP 2000-957857	20000828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000014438	A	20020820	BR 2000-14438	20000828
JP 2003510344	T2	20030318	JP 2001-527771	20000828
AU 778507	B2	20041209	AU 2000-69416	20000828
US 2002137749	A1	20020926	US 2002-106381	20020327
ZA 2002002633	A	20030225	ZA 2002-2633	20020404
US 2002173510	A1	20021121	US 2002-131236	20020425
PRIORITY APPLN. INFO.:			US 1999-409059 A	19990930
			WO 2000-US23527 W	20000828

AB The present disclosure relates to novel **compns.** which provide improved nutritional support for premenopausal and menopausal women and/or relief from symptoms associated with menopause, as well as prophylactic effects, and methods for using same. A **pharmaceutical composition** contained vitamin A 5000, vitamin D 400, vitamin E 400 IU, vitamin C 100, vitamin B1 20, vitamin B2 20, vitamin B6 25, vitamin B12 50, vitamin B3 100, folic acid 1.0, calcium carbonate 1200, copper 2, zinc 15, DHA/linolenic/linoleic acid 50/25/25 mg, and selenium 65 μg.
IT **40391-99-9 66376-36-1**, Alendronate **89987-06-4**, Tiludronate **105462-24-6**, Risedronic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** formulation for menopausal women comprising fatty acids, calcium compds., and folic acid)
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

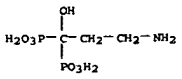
L24 ANSWER 47 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:136991 HCAPLUS
DOCUMENT NUMBER: 134:198075
TITLE: Triglyceride-free **compositions** and methods for enhanced absorption of hydrophilic therapeutic agents
INVENTOR(S): Patel, Mahesh V.; Chen, Peng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012155	A1	20010222	WO 2000-US18807	20000710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6309663	B1	20011030	US 1999-375636	19990817
CA 2380642	AA	20010222	CA 2000-2380642	20000710
EP 1210063	A1	20020605	EP 2000-947184	20000710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506476	T2	20030218	JP 2001-516502	20000710
NZ 517659	A	20041224	NZ 2000-517659	20000710
US 2001024658	A1	20010927	US 2000-751968	20001229
US 6458383	B2	20021001		
PRIORITY APPLN. INFO.:			US 1999-375636 A	19990817
			WO 2000-US18807 W	20000710

AB The present invention relates to triglyceride-free **pharmaceutical compns., pharmaceutical** systems, and methods for enhanced absorption of hydrophilic therapeutic agents. The **compns**. and systems include an absorption enhancing carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. A hydrophilic therapeutic agent can be incorporated into the **composition**, or can be co-administered with the **composition** as part of a **pharmaceutical** system. The invention also provides methods of treatment with hydrophilic therapeutic agents using these **compns.** and systems. For example, when a **composition** containing Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18, and propylene glycol 0.32 g, resp., was used, the relative absorption of PEG 4000 as a model macromol. drug was enhanced by 991%.
IT **57248-88-1**, Pamidronate disodium **66376-36-1**, Alendronate **89987-06-4**, Tiludronate **105462-24-6**, Risedronic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns.** for enhanced absorption of hydrophilic drugs using combination of surfactants)

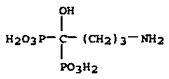
Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 47 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 57248-88-1 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

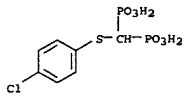


●2 Na

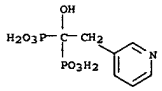
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



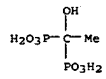
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L24 ANSWER 48 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:396514 HCAPLUS
DOCUMENT NUMBER: 135:7194
TITLE: Detergent **composition** with **controlled release** of its components
INVENTOR(S): Schmiedel, Peter; Gassenmeier, Thomas Otto; Von Rybinski, Wolfgang; Kesseler, Arnd; Hardacker, Ingo; Speckmann, Horst-Dieter; Poethkow, Jorg; Krupp, Ute
PATENT ASSIGNEE(S): Henkel Kommanditgesellschaft auf Aktien, Germany
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1103594	A2	20010530	EP 2000-125074	20001117
EP 1103594	A3	20031015		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			DE 1999-19957038	A 19991126

OTHER SOURCE(S): MARPAT 135:7194
AB Solid detergent **composition** with improved soil/stain removal capability, especially with bleachable soils and at lower washing temps., comprises an alkalizing agent, e.g., alkali carbonate, Na tripolyphosphate, etc., which is released to the washing liquor at a controlled rate. The alkalizing agent is encapsulated or compounded in such a way that ≤10% of the agent is released after t1 of 1-25 min and ≥90% is released after t1 + 3-25 min of the washing process.
IT **29329-71-3**, Sodium 1-hydroxyethane-1,1-diphosphonate
RL: TEM (Technical or engineered material use); USES (Uses)
(solid detergent **composition** with **controlled release** of alkalizing agents)
RN 29329-71-3 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, sodium salt (9CI) (CA INDEX NAME)



●x Na

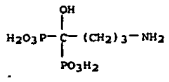
L24 ANSWER 49 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2001227030 EMBASE
TITLE: Pathogenesis and **pharmacological** treatment of bone pain in skeletal metastases.
AUTHOR: Ripamonti C.; Fulfaro F.
CORPORATE SOURCE: C. Ripamonti, Rehab. Pain Therapy/Palliative Care, National
Cancer Institute, Via Venezian 1, 20133 Milan, Italy. ripamonti@istitutotumori.mi.it
SOURCE: Quarterly Journal of Nuclear Medicine, (2001) 45/1 (65-77).
Refs: 139
ISSN: 1124-3937 CODEN: QJNMF7
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
008 Neurology and Neurosurgery
038 Adverse Reactions Titles
037 Drug Literature Index
030 Pharmacology
014 Radiology
005 General Pathology and Pathological Anatomy
023 Nuclear Medicine
036 Health Policy, Economics and Management
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Sixty-five percent of patients with advanced cancer present bone metastases and most of them present a rather slow clinical course characterized by pain, mobility deficiences and skeletal complications such as fractures and spinal cord compression. Metastatic involvement of the bone is one of the most frequent causes of pain in cancer patients and
represents one of the first signs of widespread neoplastic disease. The pain may originate directly from the bone, from nerve root compression or from muscle spasms in the area of the lesions. The mechanisms of metastatic bone pain is mainly somatic (nociceptive) even though, in some cases, neuropathic and visceral stimulations may overlap. The conventional
symptomatic treatment of metastatic bone pain requires the use of multidisciplinary therapies such as radiotherapy in association with systemic treatment (hormonotherapy, chemotherapy, radioisotopes) with the support of analgesic therapy. Recently, studies have indicated the use of bisphosphonates in the treatment of pain and in the prevention of skeletal
complications in patients with metastatic bone disease. In some patients **pharmacological** treatment, radiotherapy, radioisotopes administered alone or in association are not able to manage pain adequately. The role of neuroinvasive techniques in treating metastatic bone pain is debated. The clinical conditions of the patient, his life expectancy and quality of life must guide the physician in the choice of the best possible therapy.

L24 ANSWER 50 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:608556 HCAPLUS
DOCUMENT NUMBER: 133:198679
TITLE: Solid oral dosage form containing a permeation enhancer
INVENTOR(S): Cumming, Kenneth Iain; Ramtoola, Zebunnissa
PATENT ASSIGNEE(S): Elan Corporation, P.L.C., Ire.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050012	A1	20000831	WO 2000-GB628	20000222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2363123	AA	20000831	CA 2000-2363123	20000222
EP 1154761	A1	20011121	EP 2000-905186	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537321	T2	20021105	JP 2000-600624	20000222
US 2003091623	A1	20030515	US 2000-510560	20000222
PRIORITY APPLN. INFO.:			US 1999-121048P	P 19990222
			WO 2000-GB628	W 20000222

AB The invention relates to a solid oral dosage form comprising a **pharmaceutically** active ingredient in combination with a permeation enhancer which enhances the bioavailability and/or the absorption of the active ingredient. Accordingly, a solid oral dosage form comprises a drug and an permeation enhancer wherein the enhancer is a
medium chain fatty acid ester, ether or salt or a derivative of a medium chain
fatty acid, which is, preferably, solid at room temperature and which has a
carbon chain length of from 6 to 20 carbon atoms. Preferably, the solid oral dosage form is a **controlled-release** dosage form such as a delayed-release dosage form. The effect of sodium salts of various medium chain fatty acid on the transport of TSH releasing hormone across cultured Caco-2 cells was studied. Immediate-release tablets containing leuprolide 0.05, sodium caprate 68.82, silica 0.5, magnesium stearate 0.5, lactose 20, and disintegrant 8% were prepared
IT **66376-36-1**, Alendronate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid oral dosage form containing permeation enhancer)
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 50 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L24 ANSWER 51 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:259972 HCAPLUS
DOCUMENT NUMBER: 132:293042
TITLE: Encapsulation of sensitive liquid components into a matrix to obtain discrete shelf-stable particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): General Mills, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021504	A1	20000420	WO 1999-US20905	19991006
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2345815	AA	20000420	CA 1999-2345815	19991006
AU 9963872	A1	20000501	AU 1999-63872	19991006
AU 777977	B2	20041104		
EP 1119345	A1	20010801	EP 1999-951433	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527375	T2	20020827	JP 2000-575480	19991006

PRIORITY APPLN. INFO.:

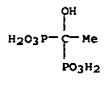
US 1998-103700P	P	19981009
US 1998-109696P	P	19981124
US 1999-233443	A	19990120
WO 1999-US20905	W	19991006

AB A liquid encapsulant component which contains an active, sensitive encapsulant, such as a live microorganism or an enzyme dissolved or dispersed in a liquid plasticizer is admixed with a plasticizable matrix material. The matrix material is plasticizable by the liquid plasticizer and the encapsulation of the active encapsulant is accomplished at a low temperature and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous process to produce discrete, solid particles. The liquid content of the liquid encapsulant component provides substantially all or completely all of the liquid plasticizer needed to plasticize the matrix component to obtain a formable, extrudable, cuttable, mixture or dough. Removal of liquid plasticizer prior to extrusion is not needed to adjust the viscosity of the mixture for formability. Release of an active component from the matrix may be delayed or controlled over time so that the active component is delivered when and where it is needed to perform its intended function. **Controlled release**, discrete, solid particles which contain an encapsulated and/or embedded component

L24 ANSWER 51 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
such as a heat sensitive or readily oxidizable **pharmaceutically**, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant.

IT **7414-83-7**, Etidronate disodium
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(encapsulation of sensitive liquid components into matrix to obtain discrete shelf-stable particles)

RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L24 ANSWER 52 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2000354618 EMBASE
TITLE: Perioperative considerations in patients with metastatic bone disease.
AUTHOR: Bibbo C.; Patel D.V.; Benevenia J.
CORPORATE SOURCE: C. Bibbo, 2840 Thornbush Court, Charlotte, NC 28270, United States
SOURCE: Orthopedic Clinics of North America, (2000) 31/4 (577-595).
Refs: 102
ISSN: 0030-5898 CODEN: OCLNAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
019 Rehabilitation and Physical Medicine
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

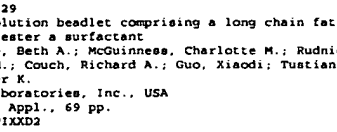
AB Preoperative assessment of patients with metastatic bone disease includes a history and physical examination, laboratory evaluation, and standard radiographs. Perioperative diagnostics include technetium bone scan, CT scans, MR imaging, positron emission tomography, and biopsy. The role of preoperative tumor embolization and vena cava filter placement is discussed in this article. Guidelines for pain control are provided. Surgical planning and instrument considerations for long bone lesions, periarticular lesions, and pelvis and acetabular lesions are addressed. The importance of rehabilitation for patients with metastatic bone disease is emphasized.

L24 ANSWER 53 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:219978 HCAPLUS
DOCUMENT NUMBER: 130:242329
TITLE: Solid solution beadlet comprising a long chain fatty acid or ester a surfactant
INVENTOR(S): Burnside, Beth A.; McGuinness, Charlotte M.; Rudnic, Edward M.; Couch, Richard A.; Guo, Xiaodi; Tustian, Alexander K.
PATENT ASSIGNEE(S): Shire Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913864	A2	19990325	WO 1998-US19658	19980918
WO 9913864	A3	19990812		
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2302275	AA	19990325	CA 1998-2302275	19980918
AU 9894967	A1	19990405	AU 1998-94967	19980918
EP 1028712	A2	20000823	EP 1998-948383	19980918
EP 1028712	B1	20050112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2001006650	A1	20010705	US 1998-156464	19980918
US 6692767	B2	20040217		
JP 2002522354	T2	20020723	JP 2000-511488	19980918
AT 286721	E	20050115	AT 1998-948383	19980918
PRIORITY APPLN. INFO.:			US 1997-59408P P	19970919
			WO 1998-US19658 W	19980918

AB Disclosed is a beadlet comprising (i) a hydrophobic long chain fatty acid or ester material; (ii) a surfactant; and (iii) a therapeutic agent, which in admixt. form a solid solution at room temperature The hydrophobic material preferably has a m.p. of about 40 to about 100°, and is most preferably glyceryl behenate. The surfactant is preferably a polyglycolyzed glyceride, polyoxyethylene sorbate, ethylene or propylene block copolymer or combinations thereof, and is most preferably polyoxyethylene 20 sorbitan monolaurate. Uncoated beadlets were prepared containing acyclovir (I) 35, Labrasol 20, Compritol 888 40, talc 5%. The transport of I through Caco-2 cell monolayers was 18.0 times the control.
IT 129318-43-0, Alendronate sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid solution beadlet comprising long chain fatty acid or ester surfactant)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 53 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

L24 ANSWER 54 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999152202 EMBASE
TITLE: Trends in cancer pain management.
AUTHOR: Lesage P.; Portenoy R.K.
CORPORATE SOURCE: Dr. R.K. Portenoy, Pain Medicine/Palliative Care Dept., Beth Israel Medical Center, First Avenue at 16th Street, New York, NY 10003, United States
SOURCE: Cancer Control, (1999) 6/2 (136-145).
Refs: 36
ISSN: 1073-2748 CODEN: CACOFD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Pain is a prevalent symptom in cancer patients, affecting up to 50% of patients undergoing active cancer treatment and up to 90% of those with advanced disease. Although adequate relief can be achieved in the majority of cancer patients, pain is often treated inadequately in traditional settings. Methods: The authors use their experience and that of others to review the evaluation and diagnosis of pain syndromes and the principles of management. Results: The World Health Organization and other governmental agencies have recognized the importance of pain management as part of routine cancer care. Conducting a comprehensive assessment, competently providing analgesic drugs, and communicating with the patient and family allow effective management of pain in the cancer patients. Conclusions: Several approaches can promote adequate management of cancer pain, such as enhancing clinician knowledge of pain syndromes, improving pain assessment, and updating medical information related to pain and symptom control.

L24 ANSWER 55 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:293427 HCAPLUS
DOCUMENT NUMBER: 129:8597
TITLE: Embedding and encapsulation of controlled release particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818610	A1	19980507	WO 1997-US18984	19971027
W: AU, CA, JP, NO, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2269806	AA	19980507	CA 1997-2269806	19971027
AU 9749915	A1	19980522	AU 1997-49915	19971027
AU 744156	B2	20020214		
EP 935523	A1	19990818	EP 1997-912825	19971027
EP 935523	B1	20040929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511777	T2	20020416	JP 1998-520558	19971027
EP 1342548	A1	20030910	EP 2003-10031	19971027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 277739	E	20041015	AT 1997-912825	19971027
NO 9902036	A	19990428	NO 1999-2036	19990428
PRIORITY APPLN. INFO.:			US 1996-29038P P	19961028
			US 1997-52717P P	19970716
			EP 1997-912825 A3	19971027
			WO 1997-US18984 W	19971027

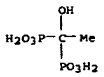
AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced

Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 55 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixt. The mixt. is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

IT 7414-83-7, Etidronate disodium
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L24 ANSWER 56 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 97263326 EMBASE
DOCUMENT NUMBER: 1997263326
TITLE: Risedronate Sodium.
SOURCE: Drugs of the Future, (1997) 22/7 (799).
Refs: 2
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:105205 HCAPLUS
DOCUMENT NUMBER: 126:122508
TITLE: Bisphosphonate cement **composition** to prevent aseptic loosening of orthopedic implant devices
INVENTOR(S): Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

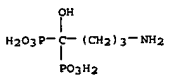
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639107	A1	19961212	WO 1996-US8515	19960603
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
RW: KE, LA, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2223450	AA	19961212	CA 1996-2223450	19960603
EP 831756	A1	19980401	EP 1996-917041	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11511041	T2	19990928	JP 1996-501089	19960603
PRIORITY APPLN. INFO.:			US 1995-470404 A	19960603
			WO 1996-US8515 W	19960603

AB Disclosed is a bisphosphonate bone cement for preventing peri-prosthetic bone loss and aseptic loosening of a joint prosthesis in patients, which cement contains a bisphosphonate bone resorption inhibitor, e.g. Na or Ca salt of alendronate and a **pharmaceutically** acceptable **polymeric carrier** such as poly(Me methacrylate). A **composition** containing Me methacrylate, N,N-dimethyl-p-toluidine, and chlorophyll was added to a **composition** containing Me methacrylate-Me acrylate copolymer, benzoyl peroxide, ZrO2, chlorophyll, and gentamicin, then alendronate Na was added to give a cement mixture

IT **185959-98-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and **polymeric carrier**)

RN 185959-98-2 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

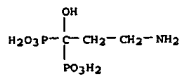


●2 Na

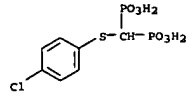
● H_2O

IT **40391-99-9 89987-06-4**, Tiludronic acid
105462-24-6 129318-43-0, Alendronate sodium
137504-89-3 157432-53-6 186090-69-7
186090-70-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and **polymeric carrier**)

RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



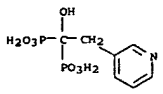
RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



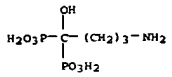
RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

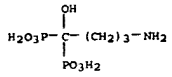


RN 129318-43-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)



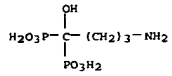
● Na

RN 137504-89-3 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (1:1) (9CI) (CA INDEX NAME)



● Ca

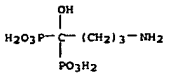
RN 157432-53-6 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, magnesium salt (9CI) (CA INDEX NAME)



●x Mg

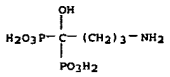
RN 186090-69-7 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, barium salt (9CI) (CA

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
INDEX NAME)



●x Ba

RN 186090-70-0 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt (2:3) (9CI) (CA INDEX NAME)

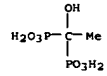


●3/2 Na

L24 ANSWER 58 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:504204 HCAPLUS
DOCUMENT NUMBER: 125:151223
TITLE: Bioabsorbable ceramic implants for bone repair
INVENTOR(S): Irie, Hiroyuki
PATENT ASSIGNEE(S): Olympus Optical Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08141067	A2	19960604	JP 1994-282035	19941116
JP 3476930	B2	20031210		
PRIORITY APPLN. INFO.:			JP 1994-282035	19941116

AB The bioabsorbable ceramic implants comprise porous β-tricalcium phosphate block and **sustained-release** bone resorption-inhibiting drug (1-hydroxyethyliden-1,1-diphosphonic acid). The ceramic implants are useful for bone repair.
IT **2809-21-4**, 1-Hydroxyethylidene-1,1-diphosphonic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioabsorbable ceramic implants for bone repair)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 59 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 96189161 EMBASE
DOCUMENT NUMBER: 1996189161
TITLE: Endocrinology.
AUTHOR: Watts N.B.; Blevins Jr. L.S.
CORPORATE SOURCE: Emory University School of Medicine,Atlanta, GA, United States
SOURCE: Journal of the American Medical Association, (1996) 275/23 (1806-1807).
ISSN: 0098-7484 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L24 ANSWER 60 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 96247146 EMBASE
DOCUMENT NUMBER: 1996247146
TITLE: Osteoporosis: The need for comprehensive treatment guidelines.
AUTHOR: Abbott III T.A.; Lawrence B.J.; Wallach S.
CORPORATE SOURCE: Pharmacoeconomics, Sandoz Pharmaceuticals Corporation, 59 Route 10,East Hanover, NJ 07936-1080, United States
SOURCE: Clinical Therapeutics, (1996) 18/1 (127-149).
ISSN: 0149-2918 CODEN: CLTHDG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
019 Rehabilitation and Physical Medicine
020 Gerontology and Geriatrics
033 Orthopedic Surgery
036 Health Policy, Economics and Management
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Osteoporosis is a debilitating disease that results in nearly 1.3 million fractures per year in the United States. The cost of treating these fractures has been estimated to be as high as $10 billion per year. These costs are expected to more than double during the next 50 years unless comprehensive programs of prevention and treatment are initiated. Both **pharmacologic** and nonpharmacologic interventions leg, diet and exercise) have been shown to have a significant impact on the incidence of osteoporosis, depending on the time of their application. Unfortunately, osteoporosis is often not diagnosed until after fractures have occurred, when it may be too late for treatment to have a major impact. To be most effective, therapy should be started early, before serious bone loss has occurred. Because of its efficacy and relatively low acquisition cost, long-term hormone replacement therapy (HRT) is considered first-line **pharmacologic** therapy for the prevention of osteoporosis. However, for various reasons, less than 25% of US women who might benefit from HRT are receiving it. Aside from HRT, the only other products approved by the US Food and Drug Administration for the treatment of osteoporosis are salmon calcitonin and alendronate. Several other agents are under development, including **sustained-release** fluoride and other products in the bisphosphonate class. The development and adoption of early detection programs and treatment guidelines are crucial to help ease the economic burden of osteoporosis. These guidelines should incorporate preventive measures such as diet and exercise, risk assessment through proper screening programs, and the appropriate use of **pharmaceutical** products. The purpose of this paper is to discuss relevant economic issues associated with osteoporosis and discuss the need for a management algorithm that could be used to more efficiently prevent and treat this disease. We conclude that further modeling is needed to determine which programs and treatments are most cost-effective within each at-risk subgroup. As clinicians better understand the need for preventive care and the advantages of the various **pharmacologic** therapies, patients with osteoporosis will receive higher-quality and more efficient medical care.

L24 ANSWER 60 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. (Continued)

L24 ANSWER 61 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 96014247 EMBASE
DOCUMENT NUMBER: 1996014247
TITLE: New drugs for osteoporosis.
SOURCE: Medical Letter on Drugs and Therapeutics, (1996) 38/965 (1-3).
ISSN: 0025-732X CODEN: MELEAP
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
033 Orthopedic Surgery
036 Health Policy, Economics and Management
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

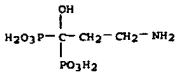
L24 ANSWER 62 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:161211 HCAPLUS
DOCUMENT NUMBER: 124:185591
TITLE: **Controlled release** oral drug delivery forms containing hydrogel-forming polymers
PATENT ASSIGNEE(S): Yissum Research Development Co., Israel
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534294	A1	19951221	WO 1995-US7519	19950613
W: AM, AT, AU, BB, BR, BY, CA, CH, CN, CZ, DE, DK, FI, GB, HU, JP, KP, RO, RU, SD, SE				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, ES, FR, GB, IT, LU, MC, SE, BF, BJ, MR, NE, SN, TD, TG				
IL 110024	A1	19980405	IL 1994-110024	19940615
AU 9528270	A1	19960105	AU 1995-28270	19950613
US 6692766	B1	20040217	US 1997-750674	19970228
US 2004185107	A1	20040923	US 2003-630918	20030731
US 2004219216	A1	20041104	US 2003-630917	20030731

PRIORITY APPLN. INFO.: IL 1994-110024 A 19940615
WO 1995-US7519 W 19950613
US 1997-750674 A1 19970228

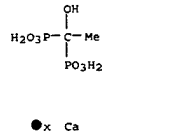
AB The present invention relates to a **controlled-release** drug delivery system comprising a drug which is susceptible to enzymic degradation by enzymes present in the intestinal tract and a polymeric matrix.
The polymeric matrix which undergoes erosion in the gastrointestinal tract comprises a hydrogel-forming polymer selected from the group consisting of (a) polymers which are themselves capable of enhancing absorption of the drug across the intestinal mucosal tissues and of inhibiting degradation of the drug by intestinal enzymes and (b) polymers which are not themselves capable of enhancing absorption of the drug across the intestinal mucosal tissues and of inhibiting degradation of the drug by intestinal enzymes. The delivery system optionally further comprises an agent which enhances absorption of the drug across the intestinal mucosal tissues and/or an agent which inhibits degradation of the drug by intestinal enzymes. For example, bradykinin was incubated with 0.5% polycarbophil suspension, then α-chymotrypsin was added to the mixture and the incubation proceeded for addnl. 120 min. Almost no degradation of bradykinin was detected.
IT **40391-99-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled-release** oral formulations containing polymeric matrix for drugs susceptible to enzymic degradation)
RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 62 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 63 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:554875 HCAPLUS
DOCUMENT NUMBER: 123:40904
TITLE: Synergism of calcium ethanehydroxybisphosphonate (CaEHBP) and FeCl3: **controlled release** polymers for preventing calcification of bioprosthetic aortic wall
AUTHOR(S): Vyavahare, Narendra R.; Qu, Xuan; Lee, Michael; Behari, Priya; Schoen, Frederick J.; Levy, Robert J.
CORPORATE SOURCE: Department of Pediatrics and Communicable Diseases, Kresge II, Room 5014, P.O.B. 0576, University of Michigan Medical School, Ann Arbor, MI, 48109-0576, USA
SOURCE: Journal of Controlled Release (1995), 34(2), 97-108
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Controlled release** delivery implants based on ethylene-vinyl acetate (EVA) copolymer were studied for prevention of calcification of aortic wall in an intracirculatory rat allograft model. The calcium salt of ethanehydroxybisphosphonate (CaEHBP) and ferric chloride (FeCl3) were used as anti-calcification drugs either in combination or sep. in solvent-cast EVA films. These matrixes were characterized in vitro for their drug release at 37°C at pH 7.4 (0.05 M HEPES buffer). Inulin was included in the single drug loaded systems as an inert filler to obtain comparable loadings. The films released the drugs in vitro continuously over 60 days without any rapid burst phase. For rat allograft studies **controlled release** matrixes or non-drug EVA films were sutured periadventitially to the aortic wall allografts to study the anticalcification efficacy for 30 days. The calcium and phosphorous levels of the explanted allografts were quantified. **Controlled release** films **releasing** both the drugs (CaEHBP and FeCl3) together synergistically inhibited calcification of the aortic walls. CaEHBP alone releasing from EVA polymer was partially effective, and EVA films releasing only FeCl3 did not inhibit calcification at all. Overall, no adverse effects on somatic growth or recipient bone morphol. were noted following **controlled release** drug administration.
IT **75323-71-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergism of calcium ethanehydroxybisphosphonate and FeCl3: **controlled release** polymers for preventing calcification of bioprosthetic aortic wall)
RN 75323-71-6 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, calcium salt (9CI) (CA INDEX NAME)

L24 ANSWER 63 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 64 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 96002869 EMBASE
DOCUMENT NUMBER: 1996002869
TITLE: Palliative care: Cancer pain management.
AUTHOR: Glare P.
CORPORATE SOURCE: Dept. of Medical Oncology/Pall. Care, Westmead Hospital,Westmead, NSW, Australia
SOURCE: Modern Medicine of Australia, (1995) 38/12 (36-51).
ISSN: 1030-3782 CODEN: MMAUB7
COUNTRY: Australia
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
016 Cancer
024 Anesthesiology
048 Gastroenterology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Intractable pain should no longer be feared as the inevitable consequence of advanced cancer. For the vast majority of patients, cancer pain can be controlled by following a four-point approach based on correct assessment of the pain mechanisms and the patient's psychological state. Reducing the noxious stimulus and attending to psychosocial problems are the cornerstones of the treatment plan. Sometimes opioid analgesics like morphine are also required. Not all types of pain responds well to opioids, and adjuvant analgesic drugs are then required. Techniques such as nerve blocks and surgery have a place in selected cases. Practicalities of each of these aspects are discussed in this article.

L24 ANSWER 65 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 94113826 EMBASE
DOCUMENT NUMBER: 1994113826
TITLE: Slow-release sodium fluoride in the management of postmenopausal osteoporosis: A randomized controlled trial.
AUTHOR: Pak C.Y.C.; Sakhaee K.; Piziak V.; Peterson R.D.; Breslau N.A.; Boyd P.; Poindexter J.R.; Herzog J.; Heard-Sakhaee A.; Haynes S.; Adams-Huet B.; Reisch J.S.
CORPORATE SOURCE: Texas Southwestern Med. Ctr. Univ., 5323 Harry Hines Boulevard, Dallas, TX 75235-8885, United States
SOURCE: Annals of Internal Medicine, (1994) 120/8 (625-632). ISSN: 0003-4819 CODEN: AIMEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To test whether intermittent treatment with slow-release sodium fluoride and continuous calcium citrate supplementation inhibits vertebral fractures without causing fluoride complications. Design: A placebo-controlled, randomized trial. Setting: Outpatient setting of specialty clinics in Dallas and Temple, Texas. Interventions: Slow-release sodium fluoride (25 mg twice daily) in repeated 14-month cycles (12 months on treatment followed by 2 months off treatment) compared with placebo. Both groups took calcium citrate (400 mg calcium twice daily) continuously. Patients: 110 patients with postmenopausal osteoporosis were randomly assigned to two groups. In the slow-release sodium fluoride group, 48 of 54 patients completed more than 1 cycle of treatment (mean, 2.44 cycles/patient), whereas 51 of 56 patients in the placebo group completed at least 1 cycle (mean, 2.14 cycles/patient) in this interim analysis. Measurements: Vertebral fracture rate and lumbar bone mineral content. Vertebral fractures were quantified from yearly radiographs. Bone mass was determined annually by densitometry. Results: In the sodium fluoride group, the mean L2 to L4 bone mineral content increased by 4% to 6% in each cycle and the mean femoral neck bone density increased by 4.1% and 2.1% during the first two cycles, but the radial bone density did not change. The placebo group showed no statistical change in bone mass at any site. Compared with the placebo group, the sodium fluoride group had a lower individual new vertebral fracture rate (0.057/patient cycle compared with 0.204/patient cycle, P = 0.017), a higher fracture-free rate (83.3% compared with 64.7%, P = 0.042), and a lower group fracture rate (0.085/patient cycle compared with 0.239/patient cycle, P = 0.006). The side-effect profile was similar for the two groups; no patient developed microfractures, hip fractures, or blood loss anemia. Conclusions: Intermittent slow-release sodium fluoride plus continuous calcium citrate, administered for about 2.5 years, inhibits new vertebral fractures, increases the mean spinal bone mass without decreasing the radial shaft bone density, and is safe to use.

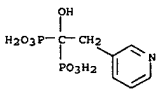
L24 ANSWER 66 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:434350 HCAPLUS
DOCUMENT NUMBER: 119:34350
TITLE: Risedronate enteric-coated **sustained-release compositions**
INVENTOR(S): Dansereau, Richard John; Mosher, Russell Youker; Axelrod, Douglas Wayne; Sietsema, William Kendall
PATENT ASSIGNEE(S): Procter and Gamble Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9309785	A1	19930527	WO 1992-US9385	19921102
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9230604	A1	19930615	AU 1992-30604	19921102
AU 661080	B2	19950713		
EP 613373	A1	19940907	EP 1992-924208	19921102
EP 613373	B1	20000802		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
JP 07501073	T2	19950202	JP 1993-509287	19921102
HU 67681	A2	19950428	HU 1994-1357	19921102
BR 9206797	A	19951031	BR 1992-6797	19921102
CZ 282760	B6	19970917	CZ 1994-1230	19921102
CA 2122479	C	19980825	CA 1992-2122479	19921102
RU 2120798	C1	19981027	RU 1994-27277	19921102
SK 279589	B6	19990111	SK 1994-595	19921102
AT 195075	E	20000815	AT 1992-924208	19921102
ES 2149781	T3	20001116	ES 1992-924208	19921102
ZA 9303337	A	19931118	ZA 1993-3337	19930513
IL 105714	A1	19970610	IL 1993-105714	19930517
FI 9402366	A	19940520	FI 1994-2366	19940520
FI 113240	B1	20040331		
NO 9401894	A	19940719	NO 1994-1894	19940520
US 5622721	A	19970422	US 1994-307495	19940914
US 5935602	A	19990810	US 1997-820430	19970312
US 6096342	A	20000801	US 1999-303466	19990430
US 6596710	B1	20030722	US 2000-591911	20000609
GR 3034373	T3	20001229	GR 2000-402060	20000908
US 2004037884	A1	20040226	US 2003-455880	20030606

PRIORITY APPLN. INFO.:
US 1991-796151 A 19911122
WO 1992-US9385 A 19921102
US 1994-307495 A1 19940914
US 1997-820430 A1 19970312
US 1999-303466 A1 19990430
US 2000-591911 A1 20000609

AB Oral enteric-coated and **sustained-release** dosage forms of risedronate are disclosed. The dosage forms protect the epithelial and mucosal tissues of the buccal cavity, pharynx, esophagus, and stomach from irritation and deliver the drug to the lower intestinal tract of the mammal. Round-shaped tablets contg. 30 mg risedronic acid Na were coated with a coating suspension contg. Eudragit L30D 33.400, PEG 1.000, talc 2.500, yellow iron oxide 0.034, simethicone emulsion 0.800, and water 75.000 mg to obtain enteric-coated **sustained-release** tablets.

IT 115436-72-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceuticals** containing, enteric-coated and **sustained-release**)
RN 115436-72-1 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt (9CI) (CA INDEX NAME)



L24 ANSWER 67 OF 79 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 94002882 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8399967
TITLE: Synergistic inhibition of the calcification of glutaraldehyde pretreated bovine pericardium in a rat subdermal model by FeCl3 and ethanehydroxydiphosphonate: preincubation and polymeric controlled release studies.
AUTHOR: Hirsch D; Drader J; Pathak Y V; Yee R; Schoen F J; Levy R J
CORPORATE SOURCE: Department of Pediatrics, University of Michigan Medical School, Ann Arbor 48109-0576.
CONTRACT NUMBER: HL 38118 (NHLBI)
SOURCE: Biomaterials, (1993 Jul) 14 (9) 705-11.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931124

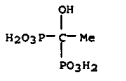
AB Calcification is a frequent cause of the clinical failure of bioprosthetic heart valves fabricated from glutaraldehyde-pretreated porcine aortic valves or glutaraldehyde-pretreated bovine pericardium (GPBP). We investigated the hypothesis that ferric chloride (FeCl3) and sodium-ethanehydroxydiphosphonate (EHDP) may act synergistically to prevent bioprosthetic tissue calcification. Pre-incubations and controlled release systems were studied individually. FeCl3-EHDP polymeric controlled release matrices were formulated using silicone rubber and evaluated for in vitro release kinetics at pH 7.4 and 37 degrees C. The effects of Fe-EHDP synergism on GPBP calcification were investigated with 21 d subdermal implants in 3 wk-old male rats. Results demonstrated that levels of Fe3+ and EHDP uptake, measured in GPBP tissues pre-incubated first in an FeCl3 solution (10(-5) M) followed by an EHDP solution (0.1 M), were higher than in the reverse order of incubation. In the first series of rat implants, GPBP was pre-incubated in either FeCl3 or Na2EHDP solutions, or sequential pre-incubations of first FeCl3 and then Na2EHDP solutions, or the reverse. The inhibition of calcification was greatest when FeCl3 (first pre-incubation, 10(-5) M) was combined with Na2EHDP (second pre-incubation, 0.1 M) (1.78 +/- 0.2 micrograms of Ca2+/mg of dried tissue) compared with the other pre-incubation groups: EHDP (first pre-incubation) combined with FeCl3 (second pre-incubation) (21.7 +/- 6.4), FeCl3 solution alone at 10(-5) M (27.9 +/- 10.7), Na2EHDP solution alone at 0.1 M (52.3 +/- 11.9) and the control group (72.3 +/- 10.2). In a second series of implants, GPBP specimens were co-implanted with individual controlled release systems containing one of the following formulations (weight percentage in silicone rubber): 1% FeCl3, 20% CaEHDP, 20% protamine sulphate, 1% FeCl3-20% CaEHDP, and 1% FeCl3-20% protamine sulphate. The 1% FeCl3-20% CaEHDP silicone-rubber matrices were the most effective for inhibiting GPBP mineralization (13.7 +/- 3.0 micrograms Ca2+/mg of dried tissue) compared with non-drug silicone co-implant controls (74.7 +/- 5.58 micrograms Ca2+/mg of dried tissue) and other polymeric treatment groups (32.3 +/- 2.3-80.0 +/- 19.7). No adverse effects on bone or overall growth of any treatment protocols were noted. Thus, combinations of FeCl3 and EHDP, using either pre-incubations or polymeric controlled release, were synergistic for inhibiting GPBP calcification.

L24 ANSWER 68 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:546496 HCAPLUS
DOCUMENT NUMBER: 119:146496
TITLE: Site-specific delivery of ethanehydroxy diphosphonate from refillable polyurethane reservoirs to inhibit bioprosthetic tissue calcification
AUTHOR(S): Johnston, T. P.; Webb, C. L.; Schoen, F. J.; Levy, R. J.
CORPORATE SOURCE: Coll. Pharm., Univ. Illinois, Chicago, IL, USA
SOURCE: Journal of Controlled Release (1993), 25(3), 227-40
CODEN: JCREEC; ISSN: 0168-3659
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Calcification (CALC) is the most frequent cause for the failure of bioprosthetic heart valves fabricated from glutaraldehyde-pretreated porcine aortic valve, and contributes to the failure of glutaraldehyde pretreated bovine pericardial (BHV) bioprosthetic heart valves as well. Although systemic therapy in rats using ethanehydroxy diphosphonate (EHDP) has proven successful in inhibiting CALC, adverse effects on serum calcium, bone development, and overall somatic growth have been noted. The present study was designed to evaluate the potential of site-specific delivery of EHDP to arrest CALC of glutaraldehyde-pretreated bovine pericardium when implanted subdermally in rats using a refillable reservoir drug delivery device. The refillable reservoir devices evaluated in these studies exhibited constant (zero-order) release of EHDP in vitro and replenishment of the drug supply when implanted subdermally in rats was achieved in a noninvasive fashion using an exteriorized entrance and exit cannula. The refillable reservoirs evaluated were fabricated from a com. available polyurethane (Biomer). Glutaraldehyde-pretreated bovine pericardium was implanted subdermally in 21-day-old rats either alone (control) or with refillable Biomer reservoirs with (treatment) or without (sham) a 2 M solution of Na2EHDP. Implanted reservoirs which initially contained a 2 M solution of Na2EHDP were refilled with a fresh 2 M solution of Na2EHDP on days 7 and 14 post-initial surgery using a syringe and the exteriorized entrance and exit cannulas. Pericardium retrieved following 21 days and assayed for calcium showed significant inhibition in CALC for tissue implanted adjacent to refillable Biomer reservoirs containing EHDP (6.9 μg/mg) compared to control (179.0 ± 13.5 μg/mg) and sham-implanted (152.0 ± 10.2 μg/mg) rats. Unimplanted pericardium had a mean tissue calcium concentration of 3.0 ± 0.5 μg/mg. Based on the in vitro release studies of EHDP from refillable Biomer reservoirs, the estimated dose delivered when implanted subdermally in rats in the present study was 5.5 ± 0.7 mg/kg per day. For rats implanted with EHDP-containing refillable reservoirs, histol. examination of retrieved pericardium and femurs from rats in each group confirmed both complete inhibition of CALC of the glutaraldehyde crosslinked pericardium and no untoward effects on bone development, resp. In addition, blood samples obtained at sacrifice showed no change in serum Ca2+ concns. in EHDP-treated animals compared to controls. Thus, the site-specific delivery of EHDP using refillable Biomer reservoirs was successful for inhibiting BHV CALC in a rat subdermal model with no untoward effects on bone development, serum Ca2+ concns., or overall growth. The advantages of the refillable reservoir system are its const. (zero-order) rate of EHDP release and its potential for replenishment of EHDP by noninvasive means when the EHDP soln. inside the reservoir has been depleted.

IT 2809-21-4
RL: BIOL (Biological study)
(controlled and site-specific delivery of, from refillable polyurethane reservoirs for inhibiting bioprosthetic heart valve calcification)

RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 69 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 93269535 EMBASE
DOCUMENT NUMBER: 1993269535
TITLE: **Controlled release** diphosphonate adventitial implants for prevention of aortic valve allograft calcifications.
AUTHOR: Qu X.; Trachy J.; Jurva J.; Underwood T.; Levy R.J.
CORPORATE SOURCE: Univ of Michigan Medical School,Ann Arbor, MI 48109-0576, United States
SOURCE: Proceedings of the Controlled Release Society, (1993) -/20 (125-126).
CODEN: 58GMAH
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L24 ANSWER 70 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 93072251 EMBASE
DOCUMENT NUMBER: 1993072251
TITLE: [Myths about dihydrocodiene as an analgesic in cancer pain].
NOCH IMMER 'BLUHEN' FALSCHE VORUTEILE. DIHYDROCODEIN ALS KREBS-SCHMERZBREMSE.
AUTHOR: Ilias W.
CORPORATE SOURCE: Abteilung fur Anasthesie, Krankenhaus der Barmherzigen Bruder, Grosse Mohrengasse 9,A-1020 Wien, Austria
SOURCE: Therapiewoche Osterreich, (1993) 8/2 (97-98+100).
ISSN: 0258-848X CODEN: THOEE6
COUNTRY: Austria
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: German
SUMMARY LANGUAGE: English; German

L24 ANSWER 71 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:520060 HCAPLUS
DOCUMENT NUMBER: 115:120060
TITLE: Disodium pamidronate double-coated granules
INVENTOR(S): Wirth, Dagmar; Bucher, Christian
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Can. Pat. Appl., 16 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2024631	AA	19910308	CA 1990-2024631	19900905
CA 2024631	C	20001121		
EP 421921	A1	19910410	EP 1990-810661	19900830
EP 421921	B1	19940427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 104856	E	19940515	AT 1990-810661	19900830
ES 2052228	T3	19940701	ES 1990-810661	19900830
IL 95558	A1	19950831	IL 1990-95558	19900831
FI 93169	B	19941130	FI 1990-4341	19900903
FI 93169	C	19950310		
US 5096717	A	19920317	US 1990-577420	19900904
DD 298049	A5	19920206	DD 1990-343841	19900905
NO 9003892	A	19910308	NO 1990-3892	19900906
NO 176646	B	19950130		
NO 176646	C	19950510		
AU 9062283	A1	19910314	AU 1990-62283	19900906
AU 623036	B2	19920430		
JP 03099016	A2	19910424	JP 1990-234618	19900906
JP 3009713	B2	20000214		
ZA 9007100	A	19910529	ZA 1990-7100	19900906
HU 59008	A2	19920428	HU 1990-5812	19900906
HU 207447	B	19930428		

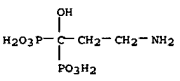
PRIORITY APPLN. INFO.: CH 1989-3245 A 19890907
EP 1990-810661 A 19900830

AB A **controlled-release** granule comprises di-Na pamidronate.5H2O (I) which is coated with a hydrophilic, elastic inner coating and a gastric juice-resistant intestinal juice-soluble outer coating.
Controlled-release granule core pellets contained I 197.3, Avicel PH105 52.7 mg/each; inner coating contained cellulose HP-M 603 10.0, polyethylene glycol 2.0, and talc 8.0 mg/each; and outer coating contained Eudragit L30D 90.0, tri-Et citrate 21.0, Antifoam AF 2.0, and talc 7.0 mg/each.

IT 109552-15-0
RL: BIOL (Biological study)
(**controlled-release pharmaceutical** granules containing)

RN 109552-15-0 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt, pentahydrate (9CI) (CA INDEX NAME)

L24 ANSWER 71 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●2 Na

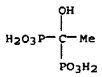
●5 H_2O

L24 ANSWER 72 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:181009 HCAPLUS
DOCUMENT NUMBER: 116:181009
TITLE: Characterization and anticalcification effects of implantable polyurethane matrixes containing amorphous dispersion of bisphosphonic acid
AUTHOR(S): Golomb, Gershon; Wagner, David
CORPORATE SOURCE: Sch. Pharm., Hebrew Univ., Jerusalem, 91120, Israel
SOURCE: Clinical Materials (1991), 8(1-2), 33-42
CODEN: CLNME2; ISSN: 0267-6605
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cardiovascular calcification, the formation of calcium phosphate deposites in cardiovascular tissue, is a common-end stage phenomenon affecting a wide variety of cardiovascular disease states and causing the dysfunction of many different types of biomaterial implants. The present investigation describes the formulation, characterization, and the in-vivo efficacy of prolonged **controlled-release** polyurethane matrixes containing the anticalcification agent 1,1-hydroxyethylidene bisphosphonic acid (HEBP). **Sustained-release** polyurethane (PU) matrixes with amorphous dispersion of the drug, in its free acid form, were obtained. Matrixes morphol. and release kinetics were solvent and concentration dependent. All HEBP matrixes (co-implanted subdermally in rats with the calcifiable bioprosthetic heart valve tissue) significantly inhibited tissue calcification (76.3 μg/mg Ca2+ in comparison to 1.1-10.1 μg/mg Ca2+, untreated and treated groups, resp.). Systemic side effects were noted only in the rats implanted with the 30% weight/weight HEBP matrixes. It is concluded that PU matrixes with amorphous dispersion of HEBP provided effective and sustained anticalcification properties.

IT **2809-21-4**
RL: BIOL (Biological study)
(anticalcification effects and **controlled release** of, from polyurethane implants)

RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

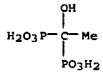


L24 ANSWER 73 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:412041 HCAPLUS
DOCUMENT NUMBER: 113:12041
TITLE: **Controlled-release** implants for cardiovascular disease
AUTHOR(S): Levy, Robert J.; Johnston, Thomas P.; Sintov, Amnon; Golomb, Gershon
CORPORATE SOURCE: Div. Pediatr. Cardiol., C.S. Mott Child. Hosp., Ann Arbor, MI, 48109, USA
SOURCE: Journal of Controlled Release (1990), 11(1-3), 245-54
CODEN: JCREEC; ISSN: 0168-3659
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The systemic therapy of many cardiovascular diseases is often hampered by adverse drug effects. The use of **controlled-release** implants as a means for optimizing drug concns. at the affected site and in the cardiovascular system, while using a relatively low systemic dose, was examined **Controlled-release** systems were prepared by combining a drug of choice with either a non-degradable polymer, such as a silicone rubber, polyurethane, and ethylene vinylacetate, or a biodegradable compound such as poly(glycolic-lactic acid) or a high-mol.-weight polyanhydride. **Controlled-release** matrixes containing ethylenehydroxydiphosphonate (EHDP), when implanted next to a bioprosthetic heart valve leaflet, prevented pathol. calcification. Similarly, **controlled-release** matrixes containing lidocaine-HCl were used exptl. as epicardial implants to convert ventricular tachycardia to normal sinus rhythm in dogs. Future **controlled-release** systems for cardiovascular use will very likely incorporate innovative design features including: a reservoir configuration to replenish or change drug therapy, modulatable drug release to vary drug dosing as desired, and closed-loop feedback to increase or decrease release rates in response to disease status.

IT **7414-83-7**
RL: BIOL (Biological study)
(polymer implants for **controlled-release** of, for cardiovascular disease treatment)

RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L24 ANSWER 74 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 3
ACCESSION NUMBER: 90089191 EMBASE
DOCUMENT NUMBER: 1990089191
TITLE: **Controlled release** of ethanehydroxy diphosphonate from polyurethane reservoirs to inhibit calcification of bovine pericardium used in bioprosthetic heart valves.
AUTHOR: Johnston T.P.; Boyd J.A.; Ciesliga B.L.; Schoen F.J.; Amidon G.; Levy R.J.
CORPORATE SOURCE: Department of Pediatrics and Communicable Disease, University of Michigan, Ann Arbor, MI 48109, United States
SOURCE: International Journal of Pharmaceutics, (1990) 59/2 (95-104).
ISSN: 0378-5173 CODEN: IJPHDE
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

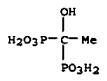
AB Calcification (CALC) of bioprosthetic heart valves (BHVs) fabricated from either glutaraldehyde-pretreated bovine pericardial tissue or porcine aortic valves is the most frequent cause of clinical failure of these devices. Previous studies have demonstrated that calcification is inhibited by diphosphonate compounds released into the vicinity of bioprosthetic tissue implanted subcutaneously in rats. **Controlled release** of the anticalcification agent ethanehydroxy diphosphonate (EHDP), as a 1:1 mixture of Na2EHDP and CaEHDP from cylindrical polyurethane (PU) reservoirs (o.d. = 0.36 cm, i.d. = 0.33 cm, length = 4 cm) fabricated by solvent casting was assessed in vitro and in vivo. The diffusivity (D), determined independently using standard diffusion cells, for ionic EHDP diffusion across the PU membrane was 1.2 x 10-10 cm2/s. Volume influx of buffer into the reservoirs in vitro was observed experimentally to reach a maximum at 7.8 days (288 ± 44μl) with a biexponential decline to 147 ± 6 μl at 70 days. The cumulative EHDP released in vitro after 70 days was 4.2 ± 0.6% (4.8 ± 0.7 mg) compared to 15.7 ± 3.2% (18.1 ± 3.7 mg) in vivo (subcutaneously in 3 week-old, male, CD rats) over 21 days. The release rate of EHDP from the reservoirs was not a zero-order process. Reservoir administration of EHDP effectively inhibited pericardial BHV-CALC in 21-day subdermal explants (Ca2+ =4.5 ± 1.4 μg Ca2+/mg tissue; control, Ca2+ =120 ± 13 μg Ca2+/mg tissue) without diphosphonate-related untoward effects at a dose of approx. 3 mg/kg per day.

L24 ANSWER 75 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 4
ACCESSION NUMBER: 89148836 EMBASE
DOCUMENT NUMBER: 1989148836
TITLE: **Controlled release** of 1-hydroxyethylidene diphosphonate: In vitro assessment and effects on bioprosthetic calcification in sheep tricuspid valve replacements.
AUTHOR: Johnston T.P.; Bove E.L.; Bolling S.F.; Boyd J.A.; Ciesliga B.L.; Amidon G.L.; Schoen F.J.; Levy R.J.
CORPORATE SOURCE: Department of Pediatrics and Communicable Disease, C.S. Mott Children's Hospital, University of Michigan Medical Center, Ann Arbor, MI 48109-0576, United States
SOURCE: International Journal of Pharmaceutics, (1989) 52/2 (139-148).
ISSN: 0378-5173 CODEN: IJPHDE
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Calcification (CALC) is the most frequent cause of the clinical failure of bioprosthetic valves (BHV's). **Controlled-release** (paravalvar) administration of the anticalcification agent ethanehydroxydiphosphonate (EHDP), as either Na2EHDP or in combination (1:1) with the less soluble CaEHDP, from a silicone rubber matrix (20% w/w EHDP) was studied both in vitro and in vivo for the prevention of BHV CALC. Seventeen sheep (6-7 months old, male, Suffolk) underwent tricuspid valve replacement using Hancock I, 25 mm porcine aortic bioprostheses. BHV explant evaluation after 16-20 weeks revealed that two of the 7 control BHV were caldified (139 ± 20.8 μg Ca2+/mg of tissue), while none of the 9 BHV retrieved from animals receiving **controlled release** EHDP demonstrated CALC (4.41 ± 1.09 μg Ca2+/mg of tissue). No adverse effects of EHDP on bone or calcium metabolism were noted. The cumulative percent of EHDP released per electron microprobe analysis was 40.4% ± 9.68 (Na, CaEHDP) to 79.0% ± 4.82 (Na2EHDP) in vivo compared to 35.7% ± 7.72 and 78.6 ± 11.1 in vitro, respectively. Assessment of the Young's modulus (Y) using thermomechanical analysis (TMA) revealed a 1.5-fold (Silastic Q7-4840) to 9.5-fold (Silastic 382) increase in Y following drug loading. The Y for explanted, Silastic Q7-4840 polymer matrices ranged from 2.84 x 104 to 5.57 x 105 dyne/cm2. In vitro osmotic related matrix swelling of the Na2EHDP loaded, unsealed matrices (20% w/w) after 75 days was minimized to a 35.8% increase in weight due to coincorporation of CaEHDP with Na2EHDP in a 1:1 ratio and was further reduced (22.2% increase in weight) by sealing 76% of the releasing surface, compared to Na2EHDP matrices which demonstrated a 414% and 141% increase in weight, respectively.

L24 ANSWER 76 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 88270653 EMBASE
DOCUMENT NUMBER: 1988270653
TITLE: Local **controlled release** of 1-hydroxyethylidene diphosphonate using silicone-rubber matrices. Effects of sterilization on in vitro release and in vivo efficacy.
AUTHOR: Johnston T.P.; Bove E.L.; Bolling S.F.; Schoen F.J.; Boyd J.A.; Golomb G.; Levy R.J.
CORPORATE SOURCE: Department of Pediatrics and Communicable Diseases, Division of Pediatric Cardiology, C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI 48109-0576, United States
SOURCE: ASAIO Transactions, (1988) 34/3 (835-838). ISSN: 0889-7190 CODEN: ASATEJ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
019 Rehabilitation and Physical Medicine
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Calcification (CALC) is the most frequent cause of the clinical failure of bioprosthetic heart valves (BHVs). **Controlled release** of disodium ethanehydroxydiphosphonate (EHDP) has been demonstrated to inhibit subdermal BHV calcification at effective low local doses, avoiding adverse effects. However, the eventual circulatory use of **controlled release** EHDP necessitates addressing several critical issues that may affect efficacy. These include the effects of sterilization on EHDP **release** and the efficacy of **sustained release** matrices containing CaEHDP, which is less soluble than NaEHDP. The effects of CaEHDP-NaEHDP incorporation and steam sterilization on **controlled release** of EHDP from silicone-rubber matrices was studied both in vitro and in vivo using a rat subdermal model and sheep tricuspid valve replacements. Autoclaved EHDP matrices (20% wt/wt) released 88.9% ± 7.84 of contained drug after 140 days in vitro, compared with control (87.6% ± 10.3 cumulative **release**). Autoclaved EHDP matrices completely inhibited BHV CALC in 60 day rat subdermal implants (8.84 ± 3.68 μg Ca++/mg tissue), comparable to nonsterilized EHDP-loaded matrices (7.06 ± 2.00 μg Ca++/mg tissue). Nontreated CALC levels were 183 ± 7.60 μg Ca++/mg tissue. Na-CaEHDP co-incorporation into silicone rubber matrices markedly prolonged **controlled release** with the 1:1 Na-CaEHDP mixture demonstrating an extrapolated release duration of approximately 20 years, assuming the total amount of dispersed drug was released. Data from tricuspid valve replacements in sheep demonstrate erratic control calcification (41.3 ± 14.9 μg Ca++/mg tissue), but complete suppression of BHV calcification with Na2EHDP **controlled release** (5.74 ± 1.35 μg Ca++/mg tissue) after 150 days.

L24 ANSWER 77 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:498604 HCAPLUS
DOCUMENT NUMBER: 109:98604
TITLE: **Controlled release** of diphosphonates from synthetic polymers to inhibit calcification
AUTHOR(S): Golomb, Gershon
CORPORATE SOURCE: Sch. Pharm., Hebrew Univ. Jerusalem, Jerusalem, 91120, Israel
SOURCE: Journal of Biomaterials Applications (1987), 2(2), 266-89 CODEN: JBAPEL; ISSN: 0885-3282
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 39 refs. on formulation and evaluation of **controlled -release** drug delivery system for diphosphonates to inhibit bioprosthetic heart valve calcification.
IT **2809-21-4D**, 1-Hydroxyethanediphosphonic acid, derivs.
RL: PROC (Process)
(**controlled release** of, from polymers, for inhibition of calcification of bioprosthetic heart valves)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 76 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. (Continued)

L24 ANSWER 78 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 5
ACCESSION NUMBER: 87036698 EMBASE
DOCUMENT NUMBER: 1987036698
TITLE: **Controlled release** of diphosphonate to inhibit bioprosthetic heart valve calcification: Dose-response and mechanistic studies.
AUTHOR: Golomb G.; Langer R.; Schoen F.J.; et al.
CORPORATE SOURCE: Department of Pediatrics, Harvard Medical School, Boston, MA 02115, United States
SOURCE: Journal of Controlled Release, (1986) 4/3 (181-194). CODEN: JCREEC
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English

Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 79 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 85192958 EMBASE
DOCUMENT NUMBER: 1985192958
TITLE: Bioefficient products. A novel delivery system.
AUTHOR: Tossounian J.L.; Mergens W.J.; Sheth P.R.
CORPORATE SOURCE: Pharmacy R & D, Hoffmann-La Roche, Nutley, NJ 07110, United States
SOURCE: Drug Development and Industrial Pharmacy, (1985) 11/5 (1019-1050).
CODEN: DDIPD8
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
048 Gastroenterology
LANGUAGE: English
AB Studies have shown that a bioefficient/HBS(TM) dosage form is more bioavailable than the conventional product. This is true with compounds which are absorbed from the upper portion of the small intestine or intended to act in the stomach contents. The increase in bioavailability is due to the design of this delivery system which is based on the HBS(TM) having a prolonged retention in the stomach, as shown by scintillation studies. Vitamins evaluated in these experiments include riboflavin, thiamine and a vitamin C plus E combination product.

L25 0 FILE MEDLINE
L26 0 FILE BIOSIS
L27 0 FILE EMBASE
L28 1 FILE HCAPLUS

TOTAL FOR ALL FILES
L29 1 L8 AND (DASCH J?/AU OR RILEY M?/AU)

Searched by: Mary Hale 571-272-2507 REM 1D86

L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:813899 HCAPLUS
DOCUMENT NUMBER: 137:299972
TITLE: Modification of the sustained-release profile of a drug by a biocompatible polymer and a bisphosphonate
INVENTOR(S): **Dasch, James R.; Riley, M. Cary I.**
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

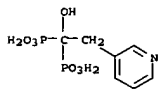
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083096	A1	20021024	WO 2002-US8440	20020319
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004100	A1	20030102	US 2001-835001	20010413
US 6558702	B2	20030506		
CA 2444421	AA	20021024	CA 2002-2444421	20020319
EP 1395240	A1	20040310	EP 2002-709857	20020319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532218	T2	20041021	JP 2002-580900	20020319
US 2003236192	A1	20031225	US 2003-400162	20030325
US 2004147488	A1	20040729	US 2004-758717	20040116
PRIORITY APPLN. INFO.:			US 2001-835001	A 20010413
			WO 2002-US8440	W 20020319
			US 2003-400162	A1 20030325

AB The present invention relates to a method for the sustained release in vivo of a biol. active agent comprising administering to a subject in need of treatment an effective amount of a sustained-release composition comprising a biocompatible polymer having the biol. active agent incorporated therein, and a bisphosphonate wherein the bisphosphonate compound is present in an amount sufficient to modify the release profile of the biol. active agent from the sustained-release composition Pharmaceutical compns. suitable for use in the method of the invention are also disclosed.

IT **2809-21-4 57248-88-1 66376-36-1**, Alendronate **89987-06-4**, Tiludronate **115436-72-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modification of sustained-release profile of drug by biocompatible polymer and bisphosphonate)

RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

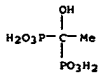
L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 57248-88-1 HCAPLUS
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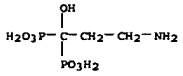
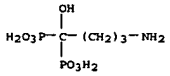
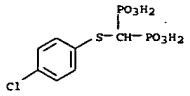


●2 Na

RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 115436-72-1 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt (9CI) (CA INDEX NAME)

Searched by: Mary Hale 571-272-2507 REM 1D86

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=> s ((sustain? or timed or control?)(4a)releas? or prolonged action) and (polymer?
carrier? or poly lactide co glycolide or polygalactin 910 or glycolic lactic acid
polyester)
L30         125 FILE MEDLINE
L31         162 FILE BIOSIS
L32         188 FILE EMBASE
L33         522 FILE HCAPLUS

TOTAL FOR ALL FILES
L34         997 ((SUSTAIN? OR TIMED OR CONTROL?)(4A) RELEAS? OR PROLONGED ACTION
                ) AND (POLYMER? CARRIER? OR POLY LACTIDE CO GLYCOLIDE OR POLYGAL
                ACTIN 910 OR GLYCOLIC LACTIC ACID POLYESTER)

=> s l34 and (compos? or pharm?)
L35          66 FILE MEDLINE
L36         154 FILE BIOSIS
L37         171 FILE EMBASE
L38         273 FILE HCAPLUS

TOTAL FOR ALL FILES
L39         664 L34 AND (COMPOS? OR PHARM?)

=> s l39 and (dasch j?/au or riley m?/au)
L40           0 FILE MEDLINE
L41           0 FILE BIOSIS
L42           1 FILE EMBASE
L43           0 FILE HCAPLUS

TOTAL FOR ALL FILES
L44           1 L39 AND (DASCH J?/AU OR RILEY M?/AU)

=> s l44 not l29
L45           0 FILE MEDLINE
L46           0 FILE BIOSIS
L47           1 FILE EMBASE
L48           0 FILE HCAPLUS

TOTAL FOR ALL FILES
L49           1 L44 NOT L29

=> d ibib abs
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Searched by: Mary Hale 571-272-2507 REM 1D86

L49 ANSWER 1 OF 1 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 97241159 EMBASE
DOCUMENT NUMBER: 1997241159
TITLE: In-vivo and in-vitro degradation of poly(lactide-co-glycolide) microspheres.
AUTHOR: Tracy M.A.; Zhang Y.; Verdon S.L.; Dong N.; Riley M.G.I.
CORPORATE SOURCE: M.A. Tracy, Alkermes Inc, Cambridge, MA 02139, United States
SOURCE: Proceedings of the Controlled Release Society, (1997) -/24 (623-624).
Refs: 3
ISSN: 1022-0178 CODEN: 58GMAH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English

Searched by: Mary Hale 571-272-2507 REM 1D86

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=> s  (dasch j?/au and riley m?/au)
L50             0 FILE MEDLINE
L51             1 FILE BIOSIS
L52             0 FILE EMBASE
L53             1 FILE HCAPLUS

TOTAL FOR ALL FILES
L54             2 (DASCH J?/AU AND RILEY M?/AU)

=> s l54 not (l29 or l44)
L55             0 FILE MEDLINE
L56             1 FILE BIOSIS
L57             0 FILE EMBASE
L58             0 FILE HCAPLUS

TOTAL FOR ALL FILES
L59             1 L54 NOT (L29 OR L44)

=> d ibib abs
```

Searched by: Mary Hale 571-272-2507 REM 1D86

L59 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:265994 BIOSIS
DOCUMENT NUMBER: PREV200300265994
TITLE: Method of modifying the release profile of sustained release compositions.
AUTHOR(S): Dasch, James R. [Inventor, Reprint Author]; Riley, M. Gary I. [Inventor]
CORPORATE SOURCE: Needham, MA, USA
ASSIGNEE: Alkermes Controlled Therapeutics, Inc.
PATENT INFORMATION: US 6558702 May 06, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 6 2003) Vol. 1270, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jun 2003
Last Updated on STN: 4 Jun 2003

AB The present invention relates to a method for the sustained release in vivo of a biologically active agent comprising administering to a subject in need of treatment an effective amount of a sustained release composition comprising a biocompatible polymer having the biologically active agent incorporated therein, and a bisphosphonate wherein the bisphosphonate compound is present in an amount sufficient to modify the release profile of the biologically active agent from the sustained release composition. Pharmaceutical compositions suitable for use in the method of the invention are also disclosed.

Searched by: Mary Hale 571-272-2507 REM 1D86

=> fil caol;s l3

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	387.29	551.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-35.04	-35.04

FILE 'CAOLD' ENTERED AT 14:28:02 ON 25 MAR 2005

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L60 10 L3

=> d 1-10

Searched by: Mary Hale 571-272-2507 REM 1D86

L60 ANSWER 1 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA65:20375f CAOLD
TI detergent-impregnated gloves
PA Trimex
DT Patent
TI washing products
PA Procter & Gamble Co.
DT Patent

PATENT NO.	KIND	DATE
PI FR 1432675		
PI NL 6517236		

IT 1643-20-5 **2666-14-0** **13502-12-0** 13502-28-8
13513-23-0 **13529-88-9**

L60 ANSWER 2 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA65:13968g CAOLD
TI detergent additives (synergistic)
PA Procter & Gamble Co.
DT Patent

PATENT NO.	KIND	DATE
PI NL 6413483		

IT 2281-11-0 **2666-14-0** **2809-21-4** 7425-12-9
13419-36-8

L60 ANSWER 3 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA65:12238d CAOLD
TI 1-hydroxyethylidenediphosphonic acid
PA Albright & Wilson (Mfg.) Ltd.
DT Patent

PATENT NO.	KIND	DATE
PI BE 672168		
NL 6514452		

IT **2809-21-4** 7316-54-3 **7414-83-7**

L60 ANSWER 4 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA65:5685a CAOLD
TI methylenediphosphonic acids (substituted)
PA Procter & Gamble Co.
DT Patent

PATENT NO.	KIND	DATE
PI GB 1026366		

IT 1660-95-3 4775-92-2 6145-32-0 **6145-33-1** 10038-58-1
10419-56-4 10595-91-2 10595-92-3 10595-93-4 10596-16-4 10596-19-7
10596-20-0 10596-21-1 10596-22-2 10596-23-3 10596-24-4 10596-26-6
10596-27-7 10596-28-8 10596-29-9 10596-30-2 10596-31-3 10596-32-4
13004-12-1 13005-02-2 **13040-51-2** 13428-84-7
13428-85-8

Searched by: Mary Hale 571-272-2507 REM 1D86

L60 ANSWER 5 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA64:8505b CAOLD
TI detergent tablets containing auxiliaries
PA Henkel & Cie G.m.b.H.
DT Patent

PATENT NO.	KIND	DATE
PI BE 650885		
FR 1408414		

IT 3794-83-0

L60 ANSWER 6 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA64:8237h CAOLD
TI phosphonic acids or their salts
PA Henkel & Cie G.m.b.H.
DT Patent

PATENT NO.	KIND	DATE
PI FR 1412865		
BE 655066		
GB 1032378		

IT 2809-21-4 3794-83-0 4712-07-6 7101-46-4***

L60 ANSWER 7 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA64:3862c CAOLD
TI chlorine-forming agents with sequestering properties
PA Monsanto Co.
DT Patent

PATENT NO.	KIND	DATE
PI NL 6407365		
BE 649996		
FR 1403179		
GB 1039966		

IT 87-90-1 1984-15-2 2244-21-5 2782-57-2 2893-78-9 6145-29-5
6145-31-9 6145-32-0 ***6145-33-1 6202-99-9 13840-33-0

L60 ANSWER 8 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA63:9991e CAOLD
TI 1-hydroxy-1,1-alkyldiphosphonic acids
AU Germscheid, Hans G.
PA Henkel & Cie G.m.b.H.
DT Patent

PATENT NO.	KIND	DATE
PI DE 1194852		
NL 6410204		

IT 2666-14-0 2809-18-9 2809-20-3 2809-21-4***

L60 ANSWER 9 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA63:4092f CAOLD
TI dyeing of human hair
PA Oreal S. A.
DT Patent
TI reduction of damage from bleaching and dyeing of hair
PA Thera-Chemie Chemisch-Therapeutische G.m.b.H.
DT Patent

PATENT NO.	KIND	DATE
PI DE 1174453		
PI GB 990660		
BE 644474		
DE 1202441		
FR 1393604		
US 3202579		1965

IT ***2809-21-4 4712-06-5 4712-07-6 4712-08-7 31182-41-9

L60 ANSWER 10 OF 10 CAOLD COPYRIGHT 2005 ACS on STN
AN CA62:4225g CAOLD
TI detergency composition
AU Diehl, Francis L.
DT Patent
TI detergents
PA Procter & Gamble Co.
DT Patent

PATENT NO.	KIND	DATE
PI US 3159581		1964
BE 651634		
BE 655988		
FR 1439824		

IT 2281-11-0 2666-14-0

Searched by: Mary Hale 571-272-2507 REM 1D86

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.83	558.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-35.04

STN INTERNATIONAL LOGOFF AT 14:28:17 ON 25 MAR 2005

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